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IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

- - -

SHIRE ORPHAN THERAPIES LLC and SANOFI-AVENTIS DEUTSCHLAND GMBH,	)	Civil Action
Plaintiffs,	)	
v.	)	
FRESENIUS KABI USA, LLC,	)	
Defendant.	)	No. 15-1102-GMS

- - -

Wilmington, Delaware
Friday, February 2, 2018
10:12 a.m.
Trial Day 4

- - -

BEFORE: HONORABLE GREGORY M. SLEET, Senior Judge, U.S.D.C., District of Delaware

APPEARANCES:

JACK B. BLUMENFELD, ESQ., and
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- - -

10:15:19 **THE COURT: Good morning, counsel. Please, take**
10:15:20 **your seats.**
10:15:22 **Let's see. Where were we?**
10:15:39 **MR. HAUG: Your Honor, good morning. Before we**
10:15:42 **call our witness, who is on direct, Dr. Wingefeld, I wanted**
10:15:46 **to bring to your attention that after Dr. Wingefeld we have**
10:15:49 **one more witness. And then the defendant's have a video**
10:15:52 **clip, a short one. And one of their other witnesses is not**
10:15:56 **coming. So there is only going to be one witness after**
10:15:59 **that. And we should be finished.**
10:16:01 **THE COURT: Okay. And we will talk about**
10:16:03 **post-evidence matters.**
10:16:27 **Good morning, Doctor.**
10:16:28 **THE WITNESS: Good morning.**
10:16:30 **... RENATE WINGEFELD, having been previously**
10:16:36 **sworn as a witness, was examined and testified further as**
10:16:39 **follows ...**
10:16:40 **THE COURT: You are still under oath.**
10:16:43 **DIRECT EXAMINATION CONTINUED**
10:16:45 **BY MR. HAUG:**
10:16:46 Q. **Good morning, Dr. Wingefeld.**
10:16:48 A. **Good morning.**
10:16:49 Q. **I would like to resume with some questions, and start**
10:16:53 **with exhibit JTX-7A, which is in Volume 1 of 3. I would**
10:17:07 **like you to please turn to JTX-7AG736.**

10:17:19 A. **Yes.**

10:17:19 Q. **Do you recognize this document?**

10:17:21 A. **Yes.**

10:17:21 Q. **What is it?**

10:17:23 A. **This is the specification, the newly signed specification we filed, we filed on February 3rd, 1993. And this is the '849 case.**

10:17:47 Q. **Thank you. Do you know how many compounds are set forth in the examples?**

10:17:53 A. **Oh, more than -- I can look it up.**

10:17:56 **More than 200.**

10:17:59 Q. **Do you know how many claims were filed in this application?**

10:18:03 A. **Yes. There were new claims, more than 30 -- yes, 34.**

10:18:14 Q. **Among those more than 200 examples, do you know which one is for icatibant?**

10:18:22 A. **The example number?**

10:18:24 Q. **Yes, please, if you know.**

10:18:26 A. **Oh, I think 59. May I double-check?**

10:18:40 **Yes. 59.**

10:18:42 Q. **Was it your goal at the time during the prosecution to get allowed claims for all of the compounds set forth in the specification?**

10:18:51 A. **Yes, all.**

10:18:51 Q. **Was it also your goal to get all of the claims that**

10:18:55 **were submitted with this application allowed?**

10:18:57 A. **Yes, it was.**

10:18:59 Q. **Was in vivo data ever submitted for all of the**

10:19:03 **compounds set forth in the examples?**

10:19:05 A. **No.**

10:19:06 Q. **Please turn to JTX-7A.124. Can you identify this**

10:19:19 **document?**

10:19:19 A. **Yes. This is a table of compounds, including IC50**

10:19:25 **data on this page for Examples 1 to 32.**

10:19:33 Q. **Thank you. Can you briefly tell us what IC50 data is?**

10:19:39 A. **IC50 data gives you the activity of a compound in an**

10:19:45 **in vitro model.**

10:19:48 Q. **So is this in vitro data set forth on this page?**

10:19:52 A. **Yes.**

10:19:52 Q. **Please turn to JTX-7A.197. Do you recognize this**

10:20:01 **document?**

10:20:06 A. **Yes.**

10:20:06 Q. **What is it?**

10:20:08 A. **Those are preliminary remarks we sent out to the**

10:20:13 **Patent Office on April 5th, 1993 in the '849 case.**

10:20:19 **THE COURT: So the record is clear, we are at**

10:20:21 **7A. Right?**

10:20:23 **MR. HAUG: Yes, Your Honor. The 7A, the A's are**

10:20:26 **just a more legible copy.**

10:20:29 **THE COURT: I understand. You said 7, and you**

10:20:31 **are making your record.**

10:20:33 **MR. HAUG: Thank you very much, Your Honor. 7.**

10:20:35 **BY MR. HAUG:**

10:20:36 Q. **I would like you to turn to the next page, JTX-7A.198.**

10:20:53 A. **Yes.**

10:20:53 Q. **Do you see, I am going to read the first couple**

10:20:58 **sentences: "By the filing of the present CIP application,**

10:21:02 **applicants do not acquiesce to any of the rejections made in**

10:21:06 **any of the pending and abandoned parent applications.**

10:21:10 **Although, to expedite prosecution, the present application**

10:21:13 **has been filed and the three pending parent applications**

10:21:16 **will be abandoned, by such action, applicants do not**

10:21:19 **acquiesce to any rejection made in any of the parent**

10:21:24 **applications and expressly reserve the right to contest the**

10:21:27 **propriety of any rejection."**

10:21:29 **Did I read that correctly?**

10:21:31 A. **Yes, you did.**

10:21:32 Q. **And what are you telling the Patent Office here?**

10:21:37 A. **We are telling the Patent Office that we want to**

10:21:40 **expedite prosecution on those cases, and that, and also we**

10:21:55 **want to -- we want to expedite, and we want to make clear**

10:22:04 **that was the reason we filed the consolidated patent**

10:22:08 **application.**

10:22:09 Q. **Please turn to JTX-7A.246. Do you recognize this**

10:22:17 **document?**

10:22:24 A. **Yes.**

10:22:25 Q. **What is it?**

10:22:27 A. **This is an office action made in the '018 case on December 6, 1994.**

10:22:35 Q. **Were all of the claims rejected?**

10:22:38 A. **Yes.**

10:22:38 Q. **Were the claims rejected for lack of utility under 101?**

10:22:43 A. **They were rejected for various reasons, and they were rejected under 101, lack of utility, yes.**

10:22:52 Q. **Did the examiner cite to the Wirth article from 1991? And I would direct your attention JTX-7A.259.**

10:23:13 A. **Yes, he did.**

10:23:14 Q. **Please turn to JTX-7A.261?**

10:23:22 A. **Yes.**

10:23:22 Q. **Is this the examiner interview summary record?**

10:23:26 A. **Yes, it is.**

10:23:27 Q. **You spoke about that last time?**

10:23:30 A. **Yes.**

10:23:31 Q. **Please turn to JTX-7A.263. Do you recognize this document?**

10:23:37 A. **Yes.**

10:23:37 Q. **What is it?**

10:23:39 A. **This is the response to the office action, and also after the interview, which took place in May, this is the**

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10:23:51 **response dated on June 6, 1995 in this '018, in the '018 case.**

10:24:01 Q. **Thank you. Please turn now to JTX-7A.298. I invite your attention to where it says the No. 2, "Rejection under 35 U.S.C. Section 101." Do you see that?**

10:24:17 A. **Yes.**

10:24:22 Q. **Did the applicant, Hoechst, disagree with the examiner's reasoning to support her 101 utility rejection throughout the prosecution of the '333 patent?**

10:24:26 A. **Yes, we did.**

10:24:31 Q. **Did the examiner ever change her position on the 101 utility rejection?**

10:24:34 A. **No. Not until this point.**

10:24:35 Q. **Was the last answer up until this point in time?**

10:24:39 A. **Yes.**

10:24:40 Q. **My question is a little broader than that. Did the examiner ever change her position on lack of utility under 101 during this prosecution?**

10:24:50 A. **Yes.**

10:24:54 Q. **That happened after this response?**

10:24:54 A. **Right.**

10:24:57 Q. **Thank you. Please go to JTX-7A.299, the next page?**

10:25:00 A. **Yes.**

10:25:02 Q. **Do you see where -- I am sorry. Do you have it?**

10:25:02 A. **Yes, I have it.**

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10:25:17 Q. **The first full paragraph, I will read this one: "According to the Guidelines For Examination of Applications For Compliance With the Utility Requirement (Fed. Reg., Volume 60, Page 98), '[a] rejection under Section 101 should not be maintained if an asserted utility for the claimed invention would be considered credible by a person of ordinary skill in the art in view of all evidence of record.'"**

Did I read that correctly?

A. **Yes.**

Q. **Now, do you recall what you were referring to by the Guidelines For Examination of Applications For Compliance?**

A. **Sorry?**

Q. **Do you recall what this is, what you are referring to here, the Guidelines for Examination?**

A. **I know what guidelines -- what those guidelines are in principle, yes.**

Q. **Please go to JTX-7A.301 and 302.**

We will start with Page JTX-7A.301?

A. **Yes.**

Q. **Do you see where there are a number of publications cited?**

A. **Yes.**

Q. **And do you know why these publications were cited here?**

10:26:40 A. **Yes.**

10:26:41 Q. **Why?**

10:26:42 A. **They were cited to further support the activity which we wanted to demonstrate that we already have shown utility in our specification.**

10:26:56 Q. **What years were those publications from?**

10:27:00 A. **Oh, those were from '94, 1993, and 1992.**

10:27:10 Q. **Please turn to JTX-7A.327. Do you recognize this document?**

10:27:29 A. **Yes, I do.**

10:27:30 Q. **What is it?**

10:27:31 A. **This is the declaration of one of the inventors, Bernward Scholkens, which was presented in this '018 case, in addition to the response to office action on June 6.**

10:27:56 Q. **Please turn to JTX-7A.329?**

10:28:01 A. **Yes.**

10:28:02 Q. **Are there any publications cited here in the Scholkens declaration?**

10:28:08 A. **Yes.**

10:28:08 Q. **What publication is cited?**

10:28:11 A. **There is cited the Wirth article, which was published in the British Journal of Pharmacology in 1992 -- in 1991, sorry.**

10:28:25 Q. **And if we go to the next page, JTX-7A.330, is there another publication cited here?**

10:28:32 A. **Yes. There is also cited another Wirth article from 1993.**

10:28:36 Q. **Is the Wirth 1991 article the same article as was earlier cited by the examiner during this prosecution?**

10:28:39 A. **Yes.**

10:28:46 Q. **Dr. Wingefeld, I am going to move now to the '7,803 patent. I am going to ask you a few questions from the smaller binder, Volume 3 of 3. First I ask you to go to DTX-059. It is at the back of the binder.**

10:28:51 A. **Yes.**

10:28:53 Q. **Do you recognize this patent?**

10:29:02 A. **Yes.**

10:29:05 Q. **What is it?**

10:29:13 A. **This is the copy of the U.S. patent 5,597,803.**

10:29:23 Q. **Did you prosecute the '803 patent?**

10:29:23 A. **Yes, I was the in-house prosecution counsel.**

10:29:26 Q. **Looking at DTX-59.1, which is the cover page of the patent, do you know when the priority application was filed for the '7,803 patent?**

10:29:26 A. **Yes. It was filed on April 4th, 1992.**

10:29:27 **It was first filed in a German priority document 4211406.3.**

10:29:36 Q. **Continuing to stay on this page, do you know when the first U.S. application was filed that led to the '7,803 patent?**

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10:30:16 A. **Yes. It was filed first on April 1st, 1993, in this**
10:30:28 **U.S. application Serial No. 41,176.**
10:30:31 Q. **If we move up to the top below the title, it says**
10:30:35 **inventors. Do you see that?**
10:30:36 A. **Yes, I see.**
10:30:37 Q. **Are the inventors the same for the '7,803 patent and**
10:30:41 **the '333 patent?**
10:30:44 A. **No. It's not the same group of inventors. I see two**
10:30:49 **additional inventors here, one is Klaus Wirth, and the other**
10:30:55 **one is Hans-George Alpermann.**
10:30:59 Q. **Who is the '7,803 patent assigned to?**
10:31:05 A. **It's assigned to Hoechst Aktiengesellschaft, or**
10:31:10 **Hoechst AG.**
10:31:10 Q. **Was the original application filed in the '333 patent**
10:31:14 **before the application was filed for the '7,803 patent?**
10:31:18 A. **Yes.**
10:31:19 Q. **Did you make a timeline to compare the '333 and the**
10:31:24 **'7,803?**
10:31:25 A. **Yes, I did.**
10:31:26 Q. **Is that in your demonstratives?**
10:31:30 A. **In the demonstratives, I think it's the very last**
10:31:36 **page. It's PDX5.9.**
10:31:45 Q. **And without reading this entire slide, what did you**
10:31:52 **want to convey with this slide?**
10:31:56 A. **I wanted to convey the timelines, the timeline from**

10:32:07 **the first prosecution, the '333 patent, and the timeline**
10:32:11 **from the prosecution of the '7,803 patent.**
10:32:15 Q. **Is the '7,803 patent in the '333 patent family?**
10:32:22 A. **No. They go -- they have different German priority**
10:32:32 **documents, and also, we received different innovation --**
10:32:40 **invention disclosure statements from the inventors.**
10:32:42 Q. **Please turn to DTX-55. It is also in your binder.**
10:32:52 **Do you recognize this document?**
10:32:54 A. **Yes. This is the file history of this U.S. patent**
10:33:01 **5,597,803.**
10:33:09 Q. **Please turn to DTX-55.73. Are you there?**
10:33:24 A. **Yes.**
10:33:24 Q. **The second paragraph, top, I will read it into the**
10:33:28 **record quickly: "Bradykinin-antagonistic peptides are**
10:33:33 **described, inter alia, in WO 86/07263 and European Patent**
10:33:40 **Applications No. 370 453, No. 413 277, No. 455 133 and No.**
10:33:52 **472 220."**
10:33:54 **Did I read that correctly?**
10:33:55 A. **Yes.**
10:33:55 Q. **Do you know what is being referenced here with the**
10:33:57 **European patent applications?**
10:33:59 A. **Yes. Here is referenced the WO 86, that's one**
10:34:08 **competitor patent application, what we think is prior art to**
10:34:12 **this application. And these three European patent**
10:34:17 **applications, 370 453, that's the European corresponding**

10:34:23 **patent application to the Group 1 of this '333 patent, the**
10:34:31 **next one, 413 277, is the European corresponding patent**
10:34:38 **application to the Group 2 peptides of the '333 patent, and**
10:34:47 **455 133 is the corresponding European patent application to**
10:34:57 **Group 3 of the '333 patent. And the last one is another**
10:35:01 **patent application from one of the competitors.**
10:35:03 Q. **So is it the case that the '333 patent disclosure was**
10:35:09 **cited in the '7,803 specification?**
10:35:11 A. **Yes.**
10:35:12 Q. **Please turn to DTX-55.155. Do you recognize this**
10:35:29 **document?**
10:35:31 A. **Yes.**
10:35:32 Q. **What is it?**
10:35:33 A. **This is an office action received for the patent**
10:35:40 **application, the '176 application. We received this on**
10:35:46 **August 24th, 1993.**
10:35:49 Q. **Did the examiner reject the claims for lack of utility**
10:35:54 **under 101?**
10:35:57 A. **Yes, he did.**
10:35:59 Q. **In that rejection did the examiner reject the claims**
10:36:02 **for lack of utility because there was no in vivo data**
10:36:07 **submitted?**
10:36:14 A. **Yes -- one second. I am sorry.**
10:36:30 **Yes. He said that the assays are not relevant**
10:36:36 **to utility in human beings.**

10:36:38 Q. **Did the examiner reject the claims under 35 U.S.C. 102(b) as anticipated by the Henke 370 453, Breipohl 455 133, and Henke 413 277 applications?**

10:36:54 A. **Yes, he did.**

10:36:55 Q. **These are all the European patent equivalents to the '333 patent. Isn't that right?**

10:37:01 A. **Yes.**

10:37:02 Q. **Please turn to DTX-55.164?**

10:37:14 A. **Yes.**

10:37:14 Q. **Do you know what this is?**

10:37:16 A. **This is an amendment we filed on February 24th, 1994 in this case. We amended the claims, which means we canceled the claims presently on file and added new claims, and also sent remarks.**

10:37:43 Q. **Please turn to DTX-55.169 through 173. If you could just quickly scan through that. My question is, does this section of your remarks respond with arguments to the examiner's rejection under 101?**

10:38:05 A. **Yes.**

10:38:06 Q. **Please turn to DTX-55.176. What is this?**

10:38:16 A. **This is now the final office action we received on May 30th 1994 in this '176 case.**

10:38:26 Q. **Were the claims still under rejection?**

10:38:29 A. **Yes.**

10:38:29 Q. **Please turn to the next page, DTX-55.177?**

10:38:35 A. **Yes.**

10:38:35 Q. **If you go down to where it says No. 3, the U.S. 35, U.S.C., 101 rejection, do you see that?**

10:38:39 A. **I see it.**

10:38:42 Q. **And I am just going to read this.**

10:38:42 **"Due to the cancellation of the rejected claims (Claims 6 and 7, which were directed to the non-statutory subject matter of intended use), this rejection is withdrawn."**

10:38:45 **Do you see that?**

10:38:57 A. **Yes, I see it.**

10:38:58 Q. **And then the next one, No. 4, if we go down one more, it says, "In view -- withdraw that.**

10:38:59 **"In view of applicant's argument, this rejection is withdrawn."**

10:39:06 **What is your understanding of what the examiner is saying there?**

10:39:09 A. **Now the examiner is saying that we presented documents, that the 101 rejection is withdrawn for the claims, Claims 9 through 11, which were on file.**

10:39:12 Q. **Was it necessary to submit any in vivo data in order to have the examiner withdraw the rejection under 101?**

10:39:14 A. **No.**

10:39:16 Q. **What was the date of this office action?**

10:39:17 A. **This was May 13th, 1994.**

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10:39:48 Q. **Please turn to DTX-55.220. What is this?**

10:40:06 A. **This is an examiner interview summary record from an interview of May 30th, 1995.**

10:40:16 Q. **Did you interview this case with the examiner?**

10:40:20 A. **Yes, I did.**

10:40:21 Q. **Was that on the same day, May 30, 1995, as you interviewed the other case?**

10:40:27 A. **Yes.**

10:40:27 Q. **I would like you to go to the last paragraph where the examiner is writing a summary. If you could please read that?**

10:40:36 A. **Okay. I will try.**

10:40:40 **"Applicants will provide declaration with data for Compounds 19 through 26 (Table, Page 25). Applicant will narrow claims to overcome 102(b) and will discuss nonobviousness of claimed compounds when compared to compounds of EP 0370 453. Applicants will show evidence of correlation of in vitro tests (Table 3, Page 27) to in vivo efficacy."**

10:41:18 **THE COURT: Doctor, did you mean "Table 1" on Page 25, the first line? I think you left out the 1, that's all.**

10:41:27 **THE WITNESS: I am sorry.**

10:41:28 **MR. HAUG: Thank you, Your Honor.**

10:41:29 **BY MR. HAUG:**

10:41:30 Q. **Thank you, Dr. Wingefeld.**

10:41:35 **Let's now go to DTX-55.237.**

10:41:44 A. **Yes.**

10:41:45 Q. **Actually, before that, did you respond to the patent**

10:41:53 **examiner after the interview?**

10:41:56 A. **Yes, we did.**

10:41:57 Q. **And did you make further arguments to overcome the**

10:42:01 **rejection over the '333 European patent disclosures?**

10:42:05 A. **Yes.**

10:42:06 Q. **Now we are on DTX-55.237. What is this document?**

10:42:11 A. **This is a notice of allowability in this '464 case,**

10:42:33 **which was issued on June 24th, 1996.**

10:42:38 Q. **Please go to DTX-55.238, the next page?**

10:42:43 A. **Yes.**

10:42:43 Q. **About halfway down, I am going to read, it says the**

10:42:49 **following: "The following is an Examiner's Statement of**

10:42:53 **Reasons for Allowance. The instant invention peptides,**

10:42:56 **methods, and compositions are neither taught nor suggested**

10:43:00 **by the prior art of record such as Henke et al. (0370453A3),**

10:43:10 **Breipohl et al., and Henke et al. (0413277A1)."**

10:43:21 **Did I read that correctly?**

10:43:22 A. **Yes.**

10:43:22 Q. **And what is your understanding of what the examiner is**

10:43:25 **saying here?**

10:43:27 A. **The examiner says that there is not the -- the '7,803**

10:43:38 **patent or invention is -- was allowed because those three --**
10:43:50 **they cite only two prior arts, and they said that those are**
10:43:56 **not prior art for the '7,803 case.**
10:44:00 Q. **What is the date again of the notice of allowability?**
10:44:03 A. **That was June 24th, 1996.**
10:44:10 Q. **Thank you. I have one last topic. That concerns**
10:44:18 **Nova. What do you know about Nova? Do you know Nova?**
10:44:21 A. **I know Nova. Nova is a pharmaceutical company. I**
10:44:31 **wrote some letters to Nova back in 1991.**
10:44:38 Q. **I am going to show you some of those letters right**
10:44:41 **now. Please turn to PTX-58 in the same binder, the small**
10:44:45 **one that you have before you?**
10:44:47 A. **Yes.**
10:44:47 Q. **Do you have it?**
10:44:48 A. **Yes, I have it.**
10:44:49 Q. **Are you familiar with this letter?**
10:44:52 A. **Yes.**
10:44:52 Q. **Is that "Dr. Wingefeld" down at the bottom, is that**
10:44:58 **your signature?**
10:44:58 A. **That is my signature.**
10:44:59 Q. **Who signed this letter next to you?**
10:45:02 A. **That is Dr. Schulze-Steinen. He was my supervisor at**
10:45:08 **that time.**
10:45:08 Q. **Was he in the Patent Department?**
10:45:11 A. **He was in the Patent Department, yes.**

10:45:13 Q. **I would like you to focus your attention on the second**
10:45:16 **paragraph, which I can read:**
10:45:19 **"We like to advise you that the above-mentioned**
10:45:22 **bradykinin antagonist has already been described in our**
10:45:25 **European Patent Application No. 370 453 published on May 30,**
10:45:30 **1990 (see especially Example 48). Since it is good general**
10:45:35 **practice to refer to the original source, we expect that you**
10:45:39 **will conform to this practice in the future."**
10:45:41 **Did I read that correctly?**
10:45:42 A. **Yes.**
10:45:43 Q. **Why did you write this letter to Nova?**
10:45:45 A. **We did this because we became aware that this**
10:45:53 **compound, a compound which was disclosed and published in**
10:45:58 **our European patent application '453, that this compound was**
10:46:06 **presented under an NPC number, which means a Nova**
10:46:13 **pharmaceutical compound, with the No. 16731 at two**
10:46:19 **conferences, one in New York in 1990, and the other one was**
10:46:25 **in London, also in 1990.**
10:46:29 Q. **Please turn to PTX-59. Do you recognize this letter?**
10:46:35 A. **Yes, I do.**
10:46:40 **That's the reply letter from Nova, in fact, from**
10:46:44 **Larry Steranka, Dr. Larry Steranka, who was vice president,**
10:46:50 **research, of Nova Pharmaceutical Corporation.**
10:46:56 Q. **Could you please just read the second paragraph into**
10:46:58 **the record?**

10:46:59 A. **Yes.**

10:47:00 **"Certainly, it is embarrassing for NOVA to be**
10:47:04 **associated with failure to acknowledge the work of others,**
10:47:07 **and we do acknowledge the importance of Hoechst's**
10:47:11 **contribution to the bradykinin field. I assure you that we**
10:47:15 **will acknowledge Hoechst in all future presentations and**
10:47:20 **publications. Please accept our apology."**

10:47:24 Q. **Please turn to PTX-60?**

10:47:27 A. **Yes.**

10:47:27 Q. **Do you recognize this letter?**

10:47:30 A. **Yes. This is another letter from Nova to myself, or**
10:47:36 **to Hoechst, from Dr. Enna, who was executive vice president.**

10:47:45 Q. **Could you just read this one?**

10:47:48 A. **Okay.**

10:47:51 **"Dear Dr. Wingefeld:**

10:47:54 **"Please accept our apology for failing to cite**
10:47:56 **the original disclosure by Hoechst of the bradykinin**
10:48:00 **antagonist," and it's D-Arg-Hyp-3-Thi-5-D-Tic-7-Tic-8 BK.**
10:48:15 **Be assured that in the future we will be more careful in**
10:48:18 **insuring that proper credit is given when referring to this**
10:48:23 **compound and other agents described in your patents. Like**
10:48:27 **you, I trust this incident will not affect our**
10:48:32 **relationship."**

10:48:32 Q. **What is the date of this letter?**

10:48:34 A. **This is March 25th, 1991.**

10:48:38 Q. **Did this exchange of letters and the apology by Nova in 1991 make you take any action to delay any of the prosecution of the '333 patent?**

10:48:48 A. **No.**

10:48:48 **MR. HAUG: No further questions, Your Honor.**

10:48:53 **THE COURT: Cross-examination.**

10:48:57 **Mr. Haug, you can collect this, because I am sure Mr. Wiesen is going to have some sort of binders.**

10:49:03 **MR. WIESEN: We will, Your Honor. With your permission, we will hand them out.**

10:49:05 **THE COURT: Except, Mr. Haug, you can leave her demonstratives with the Court.**

10:49:07 **MR. WIESEN: Your Honor, if I can take a second to explain the binders.**

10:49:40 **THE COURT: No, you can't. Let's examine the witness.**

10:49:43 **CROSS-EXAMINATION**

10:49:45 **BY MR. WIESEN:**

10:49:48 Q. **Dr. Wingefeld, we put all the prosecution histories in the big binder and all the other documents in the small ones.**

10:49:57 **THE COURT: He was determined to explain.**

10:49:58 **MR. WIESEN: I apologize, Your Honor. We will use exactly the same binders for Dr. Ellis. So we have combined everything.**

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10:50:22 **THE COURT: I told you I didn't need an**
10:50:25 **explanation, Mr. Wiesen. I meant it. Let's go.**
10:50:27 **BY MR. WIESEN:**
10:50:28 Q. **Good morning, Dr. Wingefeld.**
10:50:32 A. **Good morning.**
10:50:32 Q. **Now, when you testified on Wednesday you explained to**
10:50:40 **the Court that it was difficult at Hoechst to get in vivo**
10:50:43 **data. Is that right?**
10:50:44 A. **Yes.**
10:50:45 Q. **Because at Hoechst you weren't allowed to do in vivo**
10:50:48 **testing for every compound. Right?**
10:50:50 A. **Yes.**
10:50:50 Q. **You were only allowed to do it when there was a**
10:50:52 **particular need?**
10:50:53 A. **Yes.**
10:50:53 Q. **So you really only did in vivo testing for lead**
10:50:56 **compounds. Right?**
10:50:57 A. **Yes.**
10:50:58 Q. **So would that be just one or two compounds in any**
10:51:03 **particular program?**
10:51:04 A. **In some programs there was no other compounds. In**
10:51:09 **some programs there were a couple, yes.**
10:51:11 Q. **What is the most compounds you can remember ever**
10:51:13 **getting in vivo data on?**
10:51:17 A. **In this particular era?**

10:51:19 Q. **In this era, in the late eighties/early nineties.**

10:51:26 A. **Six, four to six, maybe, at the most.**

10:51:30 Q. **If you could turn then to DTX-59, it's going to be in the small binder because it's the '7,803 patent.**

10:51:46 A. **I am sorry?**

10:51:48 Q. **DTX-59, the '7,803 patent.**

10:51:51 A. **Yes.**

10:51:51 Q. **This was filed I think you said in 1992. Correct?**

10:51:56 A. **Yes, correct.**

10:51:57 Q. **If you turn to Table 1, it's in Column 14, which is on Page 8?**

10:52:08 A. **Yes.**

10:52:08 Q. **This is the in vivo data. Right?**

10:52:10 A. **Right.**

10:52:11 Q. **And I want to not look at all the compounds. I want to just focus on the first five, if we can pull those out?**

10:52:17 A. **Yes.**

10:52:17 Q. **For these five compounds, you would agree that a smaller number is more active, right, for IC50 data?**

10:52:33 A. **Yes, I agree.**

10:52:37 Q. **So the smallest number here is Compound 5. Right? 4.1 times ten to the negative nine?**

10:52:48 A. **For all those 16 on this?**

10:52:54 Q. **I only want to look at the first five. I don't want to go down the whole chart.**

10:52:56

10:52:58 **I have been told I may have said this is in vivo**
10:53:00 **data. I want to be clear. This is in vitro data. Right?**
10:53:03 A. **This is in vitro data.**
10:53:08 Q. **Focusing just on the first five because I don't want**
10:53:11 **to read too many, the best compound is No. 5. Right?**
10:53:15 A. **Yes.**
10:53:15 Q. **And the weakest one is No. 3 because of the ten to the**
10:53:19 **negative 8. Right? That's the biggest number?**
10:53:21 A. **Yes.**
10:53:22 Q. **If we go to the next column, 15, to Table 2?**
10:53:28 A. **Yes.**
10:53:28 Q. **If you would pull that out. This is more in vitro**
10:53:37 **data for those same five compounds. Correct? Table 2 in**
10:53:43 **Column 15 of DTX-59.**
10:53:45 A. **Yes.**
10:53:46 Q. **Again, we see that here, longer is better, right, in**
10:53:54 **this in vitro test?**
10:54:11 A. **I am not an expert in pharmacology.**
10:54:15 Q. **If we go to the text below this table, we won't focus**
10:54:20 **on the data, so Column 15, Lines 50 to 55?**
10:54:30 A. **Yes.**
10:54:31 Q. **There is in vivo data described in the '7,803 patent**
10:54:35 **as well. Right?**
10:54:35 A. **Right.**
10:54:36 Q. **It says, "Selected compounds were likewise**

10:54:39 **investigated in vivo in the test described below." Correct?**

10:54:43 A. **Yes.**

10:54:43 Q. **And then if we look for the test, it's described,**

10:54:55 **Lines 52 and 53, "Antiinflammatory effect after systemic**

10:55:00 **administration: carrageenan-induced edema of the rat paw."**

10:55:05 **Right?**

10:55:06 A. **Right.**

10:55:06 Q. **So there is in vivo data in the '7,803 patent in this**

10:55:11 **carrageenan-induced edema of the rat paw model. Right?**

10:55:15 A. **Right.**

10:55:15 Q. **And the results for that are reported in Table 3 in**

10:55:19 **Column 16. Correct?**

10:55:25 A. **I told you, I am not a pharmacologist to get this**

10:55:31 **straightened out in my mind.**

10:55:33 Q. **Do you agree these are the results from that model?**

10:55:39 A. **Yes, I agree.**

10:55:41 Q. **We don't have to get into the model.**

10:55:46 **There are six compounds reported. Right?**

10:55:48 A. **Right.**

10:55:48 Q. **Here in this patent, there is in vivo data for six**

10:55:52 **compounds?**

10:55:53 A. **Yes.**

10:55:53 Q. **And this is the only in vivo data in the '7,803**

10:55:58 **patent. Right?**

10:55:59 A. **Yes.**

10:55:59 Q. **Were all six of these compounds lead compounds for**
10:56:09 **development?**
10:56:10 A. **Pardon me?**
10:56:10 Q. **Were all six of these compounds lead compounds for**
10:56:13 **development at Hoechst in 1992?**
10:56:18 A. **I don't recall, but might be, because otherwise they**
10:56:26 **wouldn't have been tested at that time.**
10:56:28 Q. **But you don't remember?**
10:56:30 A. **No, I don't remember, because I am a member of the**
10:56:35 **Patent Department and not of the Pharmacology Department.**
10:56:40 Q. **Would you put that aside. If you turn to Exhibit 6A,**
10:56:46 **so that would be in the big binder in the prosecution**
10:56:50 **history.**
10:56:55 **We have put some tabs in the binder to direct**
10:56:57 **you to pages. We are going to go around Tab F.**
10:57:04 **That's JTX06A.221.**
10:57:10 A. **Yes.**
10:57:11 Q. **This is the February 19th, 1991 response. Correct?**
10:57:17 A. **Yes.**
10:57:19 Q. **And you pointed the Court to this document in your**
10:57:24 **direct, talking about the in vitro data should have been**
10:57:26 **enough to support utility. Right?**
10:57:28 A. **Right.**
10:57:28 Q. **You went to JTX-6 or 6A.233 there. Right? Quoted the**
10:57:43 **MPEP?**

10:57:51 A. **Yes.**

10:57:51 Q. **Along with this argument, you could have also submitted in vivo data. Right?**

10:57:55 A. **If we have no in vivo data, we could not.**

10:58:01 Q. **Well, you have in vivo data for icatibant. Right?**

10:58:03 A. **Yes.**

10:58:06 Q. **And you could have submitted that data at this date. Right?**

10:58:06 A. **They were already submitted because they were -- the Wirth article -- one second.**

10:58:11 **May I take this?**

10:58:14 **THE COURT: Sure.**

10:58:23 **THE WITNESS: Thank you.**

10:58:43 **That was for November 1st.**

10:58:45 **BY MR. WIESEN:**

10:58:52 Q. **There was no in vivo data at this time submitted?**

10:59:24 A. **Not here, no.**

10:59:25 Q. **And the very first time you actually physically submitted, gave the Patent Office in vivo data and pointed to it for the Section 101 rejection was June 6th, 1995. Right?**

10:59:25 A. **When we pointed to them, yes. But they were already on record early on.**

10:59:31 Q. **The examiner had given you a 102(f) rejection over the Wirth 1991 paper. Right?**

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11:00:04 A. **Right.**

11:00:04 Q. **And until June 6th, 1995 you never said, examiner, look at the argument, look at the evidence there, that's responsive to the 101 rejection. Correct?**

11:00:15 A. **To my understanding, this article was on the record already, and the examiner did know that there were in vivo data in this Wirth article to this compound.**

11:00:32 Q. **But you agree you never actually pointed it out, you never made that point explicitly to the examiner. Right?**

11:00:39 A. **Explicitly.**

11:00:40 Q. **Correct.**

11:00:43 A. **That there were in vivo data in this article?**

11:00:46 Q. **Yes.**

11:00:47 A. **No.**

11:00:48 Q. **You did that in June of 1995. Correct?**

11:00:54 A. **In this declaration, yes.**

11:00:56 Q. **The Scholkens declaration specifically relied on just two papers in the declaration. Right?**

11:01:05 A. **Sorry. The Scholkens --**

11:01:07 Q. **Dr. Scholkens's declaration in June of 1995 relied on only two papers. Correct?**

11:01:18 A. **Two papers, yes.**

11:01:19 Q. **He relied on the Wirth '91 paper and the Wirth '93 paper. Right?**

11:01:23 A. **Yes.**

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11:01:24 Q. **And the Wirth '91 paper was submitted in 1990. Right? Was submitted to the journal for publication in 1990. Right?**

11:01:33 A. **Yes.**

11:01:33 Q. **And the Wirth '93 paper was submitted to the journal for publication in December of '91, I believe. Right?**

11:01:41 A. **I don't know.**

11:01:41 Q. **We can look at that. It's in the record.**

11:01:45 **And that's the only data that Dr. Scholkens specifically relied on in his June 6th, 1995 declaration in response to the 101 utility rejection. Right?**

11:01:59 A. **I have to look at the declaration again.**

11:02:07 Q. **It should be Exhibit 7A, Tab H.**

11:02:12 A. **H?**

11:02:13 Q. **H.**

11:02:20 **I am going to look at Paragraph 5, which runs from 7A.329 to .330.**

11:02:50 A. **Can you please repeat?**

11:02:52 Q. **7A.329 to 330. We will put it up on the screen as well.**

11:03:21 A. **Yes.**

11:03:22 Q. **So in Paragraph 5 Dr. Scholkens explains the evidence he is relying on to conclude that the bradykinin antagonists are active in in vivo models. Correct?**

11:03:32 A. **Correct.**

11:03:32 Q. **And he cites only two papers in this paragraph.**
11:03:35 **Right?**
11:03:35 A. **Right.**
11:03:35 Q. **Wirth '91 as Exhibit 2?**
11:03:39 A. **Yes.**
11:03:39 Q. **And then further down, Wirth '93 as Exhibit 3. Right?**
11:03:46 A. **Yes.**
11:03:46 Q. **And based just on those two papers alone, he says,**
11:03:49 **"Thus, a compound that counteracts this effect of bradykinin**
11:03:54 **in vivo in an animal model can be reasonably predicted to be**
11:03:58 **effective in vivo in treating asthma."**
11:04:01 **Right?**
11:04:01 A. **Right.**
11:04:02 Q. **And he is an expert and you are providing an expert**
11:04:05 **declaration to the PTO for that. Right?**
11:04:09 A. **Right.**
11:04:09 Q. **And if we turn further in, you actually attached**
11:04:13 **copies of those papers, Wirth '91 and '93. Right?**
11:04:20 A. **Yes.**
11:04:20 Q. **Referring to JTX-7A.336. This is Wirth 1991. Right?**
11:04:33 A. **Right.**
11:04:34 Q. **And we have seen before, this was submitted to the**
11:04:38 **journal in 1990. Right?**
11:04:44 A. **Yes.**
11:04:45 Q. **And if we go to JTX-7A.342, we have a Tab I there.**

11:04:57 **That's the Wirth '93 paper. Right?**

11:05:10 A. **Yes.**

11:05:10 Q. **If we look at the very bottom left-hand corner on that**

11:05:14 **first page, we see that was received in original form**

11:05:17 **December 16, 1991. Right?**

11:05:24 A. **Yes.**

11:05:24 Q. **And this is a paper by investigators from Hoechst.**

11:05:28 **Correct?**

11:05:29 A. **Right.**

11:05:29 Q. **Including Dr. Scholkens, right, as an author?**

11:05:35 A. **Yes.**

11:05:35 Q. **Who was an inventor?**

11:05:37 A. **Correct.**

11:05:38 Q. **Who owes a duty of candor to disclose material**

11:05:41 **information during --**

11:05:43 **THE COURT: Sustained.**

11:05:43 **BY MR. WIESEN:**

11:05:44 Q. **So Hoechst had all the in vivo data that Dr. Scholkens**

11:05:51 **relied on in his January 6th, 1995 declaration by December**

11:05:56 **16th, 1991, right, all the in vivo data?**

11:06:02 A. **One in vivo data, yes.**

11:06:03 Q. **That's all the in vivo data that Dr. Scholkens relied**

11:06:07 **on in his declaration. Right?**

11:06:09 A. **Yes.**

11:06:10 Q. **And you had it all almost four years before it got**

11:06:15 **submitted with the Scholkens declaration. Right?**

11:06:19 A. **Yes.**

11:06:22 Q. **Now, when you submitted this data, you didn't give up**

11:06:25 **on your argument that in vitro data should have been enough,**

11:06:28 **did you?**

11:06:33 A. **Yes.**

11:06:34 Q. **Well, let's go back to the prosecution history, the**

11:06:38 **argument you made. We looked at some of the remarks. If we**

11:06:42 **turn to JTX-7A.298. I think it's Tab G. It's partway into**

11:06:54 **Tab G.**

11:07:01 **You looked at these pages, 298, 299, on direct**

11:07:05 **with Mr. Haug. Is that right?**

11:07:06 A. **Yes.**

11:07:06 Q. **This is where the 101 response is, in this June 6th,**

11:07:10 **1995 statement, or response to the office action. Right?**

11:07:14 A. **Right.**

11:07:14 Q. **And if we go to the next page, 299, and pull out the**

11:07:21 **whole first -- the first complete paragraph, the "According**

11:07:26 **to" paragraph. Mr. Haug read the first part of this into**

11:07:30 **the record. Right?**

11:07:31 A. **Yes.**

11:07:32 Q. **But it continues, "Applicants submit that the utility**

11:07:38 **of the claimed invention would be considered credible by one**

11:07:41 **of ordinary skill in the art on the basis of the**

11:07:44 **specification alone."**

11:07:47 **Do you see that?**

11:07:47 A. **Yes.**

11:07:48 Q. **So you continued to argue that in vitro data was enough. Right?**

11:07:51 A. **Yes.**

11:07:53 Q. **But here you didn't stop, did you? You went on and said, "However, to address the examiner's specific concerns about the predictive value of the guinea pig contractile assay, applicants submit herewith an unsigned declaration under 37 C.F.R. Section is 1.132 of Dr. Bernward Scholkens, a co-inventor of this application."**

11:07:54 **Right?**

11:08:01 A. **Yes.**

11:08:04 Q. **So here you went on and submitted the in vivo icatibant. You didn't just rest on the legal argument that in vitro was enough. Right?**

11:08:08 A. **Right. However, I want to point out that we had an invention which covers more than 200 examples, 200 compounds. We had in vivo data for just one compound. And at that time we believed it's not -- we cannot overcome the rejection with the one in vivo showing that was done -- in vivo showing was done only for one single compound. And we wanted, as always, we wanted to get all the claims allowed and all the covered compounds allowed.**

11:08:12 **So we still believed that in vitro data is**

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11:09:31 **enough to show for utility purposes.**

11:09:34 Q. **Dr. Wingefeld, you don't know why Hoechst didn't**

11:09:39 **present this argument in this response in prior applications**

11:09:44 **from the 333 prosecution, do you?**

11:09:51 A. **I don't recall why specifically we didn't do this.**

11:10:00 **However, I do know what the Hoechst practice was at that**

11:10:11 **time.**

11:10:11 Q. **But you don't actually remember, all the logic you**

11:10:15 **have given us, you don't actually remember that that applied**

11:10:18 **in this case, do you?**

11:10:21 A. **Yes. This is almost -- more than 25 years ago. I**

11:10:29 **don't recall what I specifically did in the prosecution, and**

11:10:35 **which data we did submit and which data we did not submit.**

11:10:40 **But I truly recall what the strategy was at that**

11:10:45 **time in our company.**

11:10:47 Q. **So just to be clear, you have looked back through the**

11:10:51 **prosecution history and all this material, and your**

11:10:54 **testimony is based on your reconstruction based on what you**

11:10:58 **think may have happened. Right?**

11:10:59 **THE COURT: That I think mischaracterizes her**

11:11:02 **testimony unfairly, Mr. Wiesen. I understand it's**

11:11:05 **cross-examination. But you can't do that.**

11:11:08 **MR. WIESEN: Thank you, Your Honor.**

11:11:11 **BY MR. WIESEN:**

11:11:11 Q. **You can take that down.**

11:11:34 **Can we have PDX5.3. I think, Dr. Wingefeld,**
11:11:43 **this is one of the slides you prepared but I am not sure you**
11:11:45 **went over it on direct. Do you remember this slide?**
11:11:48 A. **Yes.**
11:11:48 Q. **This was a timeline you put together of what you**
11:11:52 **called the Group 1 prosecution. Correct?**
11:11:55 A. **Yes.**
11:11:56 Q. **I want to start on the left-hand side here for a**
11:12:04 **minute. You talked about May 31st, 1991, the '162**
11:12:08 **application final office action. You got a second office**
11:12:11 **action in the '162. Right?**
11:12:20 A. **Yes.**
11:12:21 Q. **And you chose to file a CIP after that. Correct?**
11:12:31 A. **Yes, we did.**
11:12:34 Q. **You chose not to appeal the '162 final office action.**
11:12:39 **Right?**
11:12:39 A. **Yes.**
11:12:39 Q. **And you agree you can only appeal after a second**
11:12:44 **rejection. Correct? Not after the first rejection?**
11:12:47 A. **Yes -- could? I am not familiar with the U.S.**
11:12:50 **standards.**
11:12:53 **THE COURT: You are taking his word for it.**
11:12:55 **THE WITNESS: Yes.**
11:12:57 **BY MR. WIESEN:**
11:12:57 Q. **I think you testified yesterday it takes about three**

11:13:00 **years to resolve an appeal. Is that right?**

11:13:02 A. **Yes.**

11:13:03 Q. **So if you had appealed in May 31st, 1991, the appeal**

11:13:08 **would have been resolved sometime in 1994. Is that right?**

11:13:11 A. **Yes.**

11:13:12 Q. **The patent didn't actually issue until 1997. Is that**

11:13:16 **right?**

11:13:16 A. **Yes.**

11:13:31 Q. **You can take that down.**

11:13:41 **Sorry. Can you put the timeline up, PDX-5.3.**

11:13:48 **You also talked a little bit about the examiner**

11:13:51 **interview from May 30th, 1995. Do you remember that?**

11:13:55 A. **Yes.**

11:13:55 Q. **I think on Wednesday you said it was the only**

11:13:59 **interview you had. But we pointed out today there were**

11:14:02 **actually two interviews on that same day. Right?**

11:14:05 A. **Yes. The only occasion I went to the U.S. for an**

11:14:07 **examiner's interview, I think I said.**

11:14:09 Q. **And you had two interviews with two different**

11:14:12 **examiners on that same day?**

11:14:13 A. **Yes.**

11:14:13 Q. **One in the, what turned out to be the '333 and one**

11:14:17 **that turned out to be in the '7,803. Right?**

11:14:20 A. **Yes.**

11:14:21 Q. **And if we turn to 7A.261, that was the interview**

11:14:29 summary we looked at in the '333. That should be Tab F in
11:14:37 7A. We will put it up on the screen. We will pull out the
11:14:43 text here, if we can. I think you did an excellent job
11:14:46 reading it.
11:14:48 But is it fair to say that you talked about the
11:14:50 arguments that you would present in the future in this
11:14:54 interview? Correct?
11:14:56 A. That was summarized, yes.
11:14:57 Q. But you didn't actually make the arguments or present
11:14:59 the evidence here. Right?
11:15:02 A. I don't recall specifically what was talked about in
11:15:05 this interview. I can rely on -- I must rely on what this
11:15:15 record says, the summary record says.
11:15:18 Q. In fact, you even talked about the possibility of
11:15:21 filing another continuation. Right?
11:15:22 A. Yes.
11:15:22 Q. And eventually, you did file another continuation
11:15:25 before the patent actually issued. Right?
11:15:29 A. Yes, after we had submitted an amendment, a reply.
11:15:43 Q. You can take that down.
11:15:45 I want to spend a couple minutes talking about
11:15:47 the relationship with Nova.
11:15:50 A. Okay.
11:15:51 Q. You testified about some Hoechst correspondence with
11:15:55 Nova. Right?

11:15:56 A. **Right.**

11:15:56 Q. **It was in PTX-58, if we turn there, please. We will put it on the screen, Dr. Wingefeld. It is a short one.**

11:16:05 A. **Okay.**

11:16:06 Q. **This was the February 26th, 1991 letter that you wrote. Right?**

11:16:12 A. **Yes.**

11:16:13 Q. **And you identified that Nova had recently published on a compound that they numbered NPC No. 16731. Right?**

11:16:23 A. **Right.**

11:16:23 Q. **And you gave the structure of it. Correct?**

11:16:25 A. **Yes.**

11:16:26 Q. **And I am just going to describe it as the D-Tic7-Tic-8 compound, if that's okay?**

11:16:34 A. **Yes, that's okay.**

11:16:38 Q. **Now, you know, by this point you knew that Nova had published data on NPC 16731. Right?**

11:16:49 A. **I knew that they presented something, yes.**

11:16:53 Q. **And if we turn to the next page, PTX-58.2, there is actually an article by Steven Farmer, who had been at Nova, attached to your letter. Correct?**

11:17:07 A. **Yes.**

11:17:07 Q. **If we turn to PTX-58.7, pull out the bottom paragraph, they report that the activity of NPC 16731 is better than the activity of NPC 567. Right?**

11:17:25

11:17:30 A. **Yes.**

11:17:30 Q. **So you knew all of that by February of 1991 at Hoechst. Correct?**

11:17:35 A. **Yes.**

11:17:36 Q. **Now, you told the Nova folks to go look at your European patent. Right?**

11:17:41 A. **Yes.**

11:17:42 Q. **And that the compound was disclosed there?**

11:17:43 A. **Right.**

11:17:45 Q. **If you look at, in your binder it should be PTX-357, it's in the small binder because it's a patent application, not the prosecution history. Sorry. PTX-357?**

11:17:45 A. **Yes.**

11:17:56 Q. **That's all the European application, 0 370 453. Right?**

11:18:00 A. **Yes.**

11:18:09 Q. **I think you may have looked at this?**

11:18:09 A. **Yes.**

11:18:14 Q. **If we turn to 357.17, Example 48?**

11:18:15 A. **Yes.**

11:18:16 Q. **That's that same D-Tic-Tic compound. Right?**

11:18:19 A. **Yes.**

11:18:19 Q. **So this is what you were saying: We have published NPC 16731 in our patent application before you, Nova, published your papers. Right?**

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11:18:47 A. **Yes.**

11:18:48 Q. **If we turn back, however, to Page PTX-357.1 -- I am sorry, .10, Table 1 here is the activity data. Right?**

11:18:57 **THE COURT: Hold on.**

11:19:07 **THE WITNESS: Yes.**

11:19:10 **BY MR. WIESEN:**

11:19:11 Q. **And this is in vitro data only?**

11:19:12 A. **Yes.**

11:19:16 Q. **And will you take my word on it that that compound, Example 48, is not contained in this table?**

11:19:16 **There is one D-Tic-Tic compound. It's about halfway down, a little bit more, but it's different in the 2 and 3 position?**

11:19:21 A. **Yes.**

11:19:27 Q. **So in the prior Hoechst patent application, there was no data for 16731, right? Just the structure?**

11:19:29 A. **Yes.**

11:19:33 Q. **That was true in the original U.S. application, correct, as well, in June 30, 1989, there was no data for this NPC 16731 compound. Right?**

11:19:34 A. **Right.**

11:19:35 Q. **But you later -- later it was added into the -- well, let's look at a couple things Hoechst did.**

11:19:42 **I want to go to the U.S. patent prosecution then to JTX-6A.256.**

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11:20:35 **It's in Tab G of 6A?**

11:20:44 A. **Sorry. 6A?**

11:20:47 Q. **.256.**

11:21:00 A. **Yes.**

11:21:01 Q. **And this is a supplemental information disclosure statement. Correct?**

11:21:06 A. **Yes.**

11:21:06 Q. **And if we go to the next page, it was submitted August 14th, 1991. Right?**

11:21:13 A. **Right.**

11:21:13 Q. **And that's after you had seen the Nova publications on data for NPC 16731, because we saw that in February of 1991.**

11:21:27 A. **Yes.**

11:21:28 Q. **And if we go to the first page of this, Entry 1, do you recognize this as the Kyle article that's been -- that's marked as JTX-9? It's an article by people from Nova. Correct?**

11:21:46 A. **Yes.**

11:21:47 Q. **About that same compound?**

11:21:48 A. **Yes.**

11:21:49 Q. **So you gave it to the Patent Office after you had seen the data from Nova. Right?**

11:21:55 A. **Right.**

11:21:55 Q. **And you also added data about that compound into your patent after you had seen that Nova had data on the**

11:22:00

11:22:04 **compound. Right?**

11:22:06 A. **We added data later on to -- more than this compound**

11:22:12 **to the patent, yes.**

11:22:14 Q. **If you go to JTX-6A.323, which is Tab H?**

11:22:28 A. **Yes.**

11:22:28 Q. **This is the preliminary amendment from the '149**

11:22:33 **application?**

11:22:33 A. **Yes.**

11:22:33 Q. **And it's filed in 1991. Right?**

11:22:36 A. **Yes.**

11:22:38 Q. **And if you turn to Page JTX-6A.328?**

11:22:44 A. **Yes.**

11:22:44 Q. **This is some of the data that you add in the**

11:22:50 **continuation-in-part. Right?**

11:22:51 A. **Right.**

11:22:51 Q. **And we see here now data for Example 48. Right?**

11:22:56 A. **Yes.**

11:22:56 Q. **But you didn't have any data in the patent for NPC**

11:23:00 **16731 until after you saw that Nova had generated data on**

11:23:05 **the compound and published on it?**

11:23:07 A. **There were no data on this compound in the**

11:23:11 **specification before, yes.**

11:23:12 Q. **You can take that down then.**

11:23:23 **I want to go to the prosecution history for the**

11:23:25 **'7,803. That is in the big binder, because it's a**

11:23:28 **prosecution history. It's DTX-55.**

11:23:31 A. **Okay.**

11:23:32 Q. **Unfortunately, it's in the back of that binder.**

11:23:44 **You prosecuted this patent?**

11:23:45 A. **Yes.**

11:23:46 Q. **Or technically you supervised U.S. lawyers prosecuting**

11:23:50 **the patent?**

11:23:51 A. **Yes.**

11:23:51 Q. **And we looked at the notice of allowance, or you**

11:23:55 **looked at the notice of allowance with Mr. Haug, it's**

11:23:59 **DTX-55.237. If we pull up the first line there, it refers**

11:24:11 **to preliminary amendments on 1/17/95 and 9/18/95. Right?**

11:24:19 A. **Right.**

11:24:19 Q. **Let's go back to that second preliminary amendment,**

11:24:23 **the last thing you filed before the notice of allowance. I**

11:24:26 **think it's PTX-55.221.**

11:24:40 A. **Yes.**

11:24:41 Q. **You talked about the interview before this and the**

11:24:43 **notice of allowance, but not this document with Mr. Haug.**

11:24:48 **Right?**

11:24:49 A. **We talked about this interview, yes.**

11:24:52 Q. **If you turn in 55.226, at the bottom you are**

11:25:03 **responding to a 102 -- DTX.226?**

11:25:15 A. **Yes, I have it.**

11:25:17 Q. **If we can get it up on the screen.**

11:25:28 **At the very bottom you are responding to a**
11:25:30 **102(b) rejection. Right?**
11:25:34 A. **Right.**
11:25:34 Q. **That is the question of whether the compounds of the**
11:25:38 **'333 patent render invalid the compounds of the '7,803**
11:25:44 **patent. Right?**
11:25:45 A. **Right.**
11:25:45 Q. **So the question the examiner is looking at is whether,**
11:25:49 **if you start with icatibant, is Fmoc icatibant obvious.**
11:25:56 **Right?**
11:25:57 **MR. HAUG: Objection, Your Honor. That is a**
11:25:58 **characterization of what may or may not have happened.**
11:26:01 **THE COURT: Okay. Sustained. Rephrase.**
11:26:03 **BY MR. WIESEN:**
11:26:03 Q. **The examiner here is looking at the compounds of the**
11:26:08 **'333 application or the European priority one, whether those**
11:26:13 **render invalid the compounds claimed in the '7,803 patent.**
11:26:18 **Right?**
11:26:19 A. **Yes.**
11:26:19 Q. **The examiner is not looking at whether the compounds**
11:26:23 **of the '7,803 patent render invalid the compounds of the**
11:26:27 **'333 patent. Right?**
11:26:32 A. **Yes.**
11:26:33 Q. **If we go to the next page, and we pull out the first**
11:26:43 **full -- the second full paragraph that says "The compound of**

11:26:48 **the invention?"**

11:26:49 A. **Yes.**

11:26:50 **May I add something to my last response?**

11:26:53 Q. **Mr. Haug will have an opportunity.**

11:26:55 A. **Okay, sorry.**

11:26:56 Q. **You wrote in the last thing submitted in the '7,803 prosecution, "The compounds of the invention differ from those of prior are" -- I think it should be "art," not "are." Right?**

11:27:11 A. **Yes.**

11:27:11 Q. **"The compounds of the invention differ from those of the prior art because they have at the N-terminus a large lipophilic residue that can, but need not, function as a protective group. For example, Fmoc is a protective group according to the invention, and Fmoc differs from the acetyl group disclosed in the prior art references."**

11:27:33 **Do you see that?**

11:27:34 A. **Yes, I see it.**

11:27:35 Q. **So you told the PTO that Fmoc could function as a protective group in the '7,803 patent. Right?**

11:28:02 A. **That's one number what Fmoc can be, can be a protective group, yes. It can be, but it must not be a protective group.**

11:28:12 Q. **It can be a protective group but it can not be a protective group. Right?**

11:28:17 A. **Right.**

11:28:18 Q. **And you are not -- that's what you are telling the examiner here?**

11:28:21 A. **Yes.**

11:28:22 Q. **If we go to the two paragraphs underneath this.**

11:28:37 **You are talking about here then whether there are unexpected results with the Fmoc protective groups. Correct?**

11:28:45 A. **With the Fmoc group.**

11:28:48 Q. **It's actually any of a different acetyl groups or Fmoc, right, because there is a series of groups that can go in that Z. Do you remember that?**

11:28:58 A. **There are many of those groups that can get in.**

11:29:03 Q. **Let me do it this way to make sure it's very specific. If you turn to the next page, DTX-55.228. Pull out the table?**

11:29:13 A. **Yes.**

11:29:13 Q. **These are some of the compounds that are claimed in the '7,803 patent, the five examples. Correct?**

11:29:20 A. **Correct.**

11:29:21 Q. **And what you are you were arguing here is that the results for these compounds were better than the results for icatibant, and that was unexpected. Right?**

11:29:34 A. **For the purpose of the '7,803 patent application better.**

11:29:41

11:29:41 Q. **And it was unexpected that they were better. Correct?**

11:29:45 A. **Correct.**

11:29:45 Q. **And so without the data, a person would have expected that icatibant is better than Fmoc icatibant. Right?**

11:29:56 **MR. HAUG: Objection. That is a question that is not even connected to this file history. That is asking for expert opinion.**

11:30:04 **THE COURT: That's, I think, the gravamen of your objection. Mr. Wiesen, do you understand?**

11:30:11 **MR. WIESEN: I do. And I will tie it back.**

11:30:14 **BY MR. WIESEN:**

11:30:15 Q. **If we can go back to the prior page and pull out this bottom paragraph, it says -- now we are on DTX-55.227, it says, "Applicants have informed the undersigned that the duration of action (T50) of HOE140, a prior art compound with an N-terminal acetyl group, is 51 minutes."**

11:30:41 **HOE140 is icatibant?**

11:30:42 A. **Yes.**

11:30:42 Q. **So we have got 51 minutes for icatibant. Right?**

11:30:48 A. **Right.**

11:30:48 Q. **If you go to the next page, DTX-55.228, Compound 1, would you agree with me, is Fmoc, and then the sequence for icatibant?**

11:31:00 A. **Yes.**

11:31:01 Q. **And so the comparison here is icatibant to a series of**

11:31:06 **compounds that includes Fmoc icatibant. Right?**

11:31:15 A. **Yes, three of them, yes.**

11:31:16 Q. **And if we look at the paragraph underneath Table 2 on**
11:31:20 **DTX-55.228, you wrote, "As one of ordinary skill in the art**
11:31:26 **would not have expected these compounds to show a greater**
11:31:29 **duration of action, these results represent an unexpected**
11:31:33 **improvement over the prior art."**

11:31:36 **Right?**

11:31:36 A. **Right.**

11:31:37 Q. **So your conclusion is that Fmoc icatibant is better**
11:31:41 **than icatibant. Correct?**

11:31:44 A. **Yes, for this purpose, yes.**

11:31:47 Q. **But that was unexpected?**

11:31:48 A. **Yes.**

11:31:48 Q. **Which means that before someone saw this data they**
11:31:52 **would have expected icatibant to be better than Fmoc**
11:31:56 **icatibant. It turns out that's wrong. But that's what they**
11:31:59 **would have expected. Right?**

11:32:03 **MR. HAUG: Objection to that question.**

11:32:05 **THE COURT: Sustained.**

11:32:11 **You don't have to answer. He is asking you for**
11:32:13 **an expert opinion.**

11:32:16 **THE WITNESS: Thank you.**

11:32:17 **MR. WIESEN: You can take that down.**

11:32:19 **BY MR. WIESEN:**

11:32:19 Q. **Now, Dr. Wingefeld, the '7,803 patent application was**
11:32:32 **never disclosed during the '333 prosecution. Right?**
11:32:37 A. **Yes.**
11:32:38 Q. **You never told the examiner in the '333 prosecution**
11:32:44 **that you had another application to other compounds -- to**
11:32:49 **these other compounds in the '7,803. Right?**
11:32:52 A. **Yes.**
11:32:52 Q. **You went to two interviews on May 30th, 1995.**
11:32:56 **Correct?**
11:32:57 A. **Yes.**
11:32:57 Q. **With two different examiners. Right?**
11:32:59 A. **Yes.**
11:33:00 Q. **And at one of the interviews you talked about whether**
11:33:03 **the compounds of the '333 patent rendered invalid the**
11:33:09 **compounds claimed in the '7,803 patent. Right?**
11:33:12 A. **Yes.**
11:33:12 Q. **And then in the interview about the '7,803 patent, you**
11:33:17 **didn't even mention the compounds of the -- sorry, in the**
11:33:20 **interview about the '333 patent, you didn't mention the**
11:33:24 **existence of the compounds about the '7,803. Right?**
11:33:34 A. **I don't recall if we mentioned it. But it's not in**
11:33:38 **the records.**
11:33:39 Q. **Now, looking at your chart of the prosecution history,**
11:33:44 **you combined the Group 1, Group 2 and Group 3 patents into**
11:33:50 **the '849. Correct?**

11:33:52 A. **Yes.**

11:33:52 Q. **And you did that, I think you testified, because there were ODP rejections. Right?**

11:33:56 A. **Right.**

11:33:59 Q. **Obviousness-type double patenting rejections. Right?**

11:34:00 A. **Yes.**

11:34:03 Q. **You never provided a scientific response to those obviousness-type double patenting rejections. Right?**

11:34:04 A. **I am sorry, what is a scientific --**

11:34:07 Q. **You overcame those objections by combining everything into one application so that there weren't multiple applications to reject over. Right?**

11:34:15 A. **Yes.**

11:34:18 Q. **You never argued the examiner's logic is incorrect on the obvious-type double patenting rejection?**

11:34:21 A. **From reviewing the file history, we did this before in this specific Group 3 and Group 2, and when those groups were separated.**

11:34:23 Q. **But you never did it in the Group 1 claims. Right?**

11:34:41 A. **I don't know now.**

11:34:45 Q. **Let's look at one of those obviousness-type double patenting rejections. It's JTX6A.474. It's in Tab I.**

11:34:55 **Just for context, this is a July 1, 1992 rejection. If you go back to the beginning of Tab I, if you need to see it.**

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11:35:57 A. **Okay. Yes. I see it.**

11:35:59 Q. **And if you turn -- we are on JTX-6A.474, the paragraph that begins "Claims 5 through 17 are provisionally rejected."**

11:36:14 A. **Yes, I see that.**

11:36:15 Q. **This was one of the obviousness-type double patenting rejections you received?**

11:36:16 A. **Right.**

11:36:20 Q. **This was in one of the Group 1 applications. Right?**

11:36:22 A. **Yes.**

11:36:24 Q. **And the objection was over, I think it's one of the Group 2 applications. Correct? The '270?**

11:36:27 A. **Yes.**

11:36:32 Q. **And the examiner wrote, "Although the conflicting claims are not identical, they are not patentably distinct from each other because the difference seen, i.e., D-Phe of the claimed peptide sequence as opposed to the co-pending D-Tic does not constitute a patentable distinction as these residues are obvious variants, both belonging to the same class of D-aromatic amino acid residues."**

11:36:32 **Do you see that?**

11:36:37 A. **Yes, I see it.**

11:36:40 Q. **And you at Hoechst overcame this rejection by combining all the applications together. Correct?**

11:36:46 A. **Yes.**

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11:37:11 Q. **You never presented an argument to the examiner that said, this logic, this scientific logic, is incorrect. Right?**

11:37:19 A. **I would have to read all of my responses.**

11:37:24 Q. **Let me ask it a different way. If you filed that response, we would find it in the prosecution histories. Right?**

11:37:28 A. **Right.**

11:37:36 **MR. WIESEN: No further questions, Your Honor.**

11:37:37 **THE COURT: Mr. Haug.**

11:37:39 **REDIRECT EXAMINATION**

11:37:40 **BY MR. HAUG:**

11:37:41 Q. **Just a very few questions, Dr. Wingefeld.**

11:37:42 **Moments ago you were looking at the '7,803 file history. Do you remember that?**

11:37:57 A. **Yes.**

11:38:00 Q. **And Mr. Wiesen was taking you to the comparison between the compounds that were contained in the '7,803 with icatibant. Right?**

11:38:01 A. **Right.**

11:38:01 Q. **Do you know if icatibant has an acetyl group attached to it?**

11:38:05 A. **Yes, it has.**

11:38:11 Q. **Mr. Wiesen also asked you about the '7,803 and asked you whether it was disclosed in the '333 patent. Do you**

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11:38:35 remember that?
11:38:36 A. I am sorry. Can you please repeat?
11:38:40 Q. I believe your testimony is that the '7,803 patent was not mentioned or disclosed during the '333 patent prosecution?
11:38:51 A. Yes.
11:38:51 Q. He didn't ask you why. So I am going to ask you why. Why was the '7,803 patent not disclosed during the '333 patent prosecution history?
11:38:59 A. The '7,803 patent application was filed about four years after the '333 patent was filed in the U.S., so the '7,803 patent is not prior art over the '333 patent, and that's the reason why we didn't -- that's why it was not disclosed.
11:39:01 MR. HAUG: Thank you. No further questions. Thank you, Dr. Wingefeld.
11:39:33 THE COURT: Thank you, Doctor. Be careful stepping down.
11:39:35 THE WITNESS: Thank you.
11:39:36 (Witness excused.)
11:39:38 THE COURT: What do we have next?
11:39:39 MR. HAUG: Plaintiffs call Dr. Joan Ellis.
11:39:45 THE COURT: Is this by video?
11:39:53 MR. HAUG: No.
11:39:58 THE COURT: Okay.
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11:40:02 **MR. HAUG: This will be our last witness, Your Honor.**

11:40:04

11:40:36 **... JOAN ELLIS, having been duly sworn as a witness, was examined and testified as follows ...**

11:40:47

11:40:57 **THE COURT: Good morning, Doctor.**

11:41:00 **THE WITNESS: Good morning.**

11:41:03 **THE COURT: All right.**

11:41:03 **DIRECT EXAMINATION**

11:41:04 **BY MR. HAUG:**

11:41:05 Q. **Good morning, Dr. Ellis.**

11:41:23 A. **Good morning.**

11:41:25 Q. **Where are you currently employed?**

11:41:31 A. **I am employed at Dickinson Wright PLLC.**

11:41:35 Q. **And you have -- you should have a binder in front of you with some demonstrative exhibits in it. Do you see that?**

11:41:41

11:41:41 A. **I do, yes.**

11:41:42 Q. **Did you prepare these demonstratives?**

11:41:45 A. **Yes, I did.**

11:41:46 Q. **If you would turn to PDX6.1, can you briefly describe your educational background?**

11:41:52

11:41:53 A. **Yes. In 1973 I received a Bachelor's degree in microbiology from Southern Illinois University. And then in 1983 I received a Ph.D. in molecular parasitology and biochemistry from New York University School of Medicine.**

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11:42:13 **And then in 1992 I received a J.D. at George Washington**
11:42:20 **University School of Law.**
11:42:22 Q. **Please turn to PTX-65. Are you familiar with this**
11:42:27 **document?**
11:42:28 A. **Yes, I am.**
11:42:30 Q. **What is it?**
11:42:31 A. **It is my CV.**
11:42:33 Q. **Is your CV up to date?**
11:42:35 A. **Yes, it is.**
11:42:36 Q. **Could you now briefly describe your professional**
11:42:39 **experience immediately following your Ph.D.?**
11:42:43 A. **Immediately after my Ph.D., I was a research fellow at**
11:42:49 **the New York University School of Medicine, and then I took**
11:42:55 **a junior faculty position at the Rockefeller University. In**
11:42:59 **both of those jobs I was doing research in molecular**
11:43:04 **science.**
11:43:05 **Then in 1987 I joined the U.S. PTO as a patent**
11:43:10 **examiner, and I was a patent examiner there for about eight**
11:43:14 **years. And then in 1995 I was promoted to be an APJ at the**
11:43:22 **U.S. PTO.**
11:43:22 Q. **How long were you at the U.S. PTO?**
11:43:25 A. **Over 20 years -- almost 20 years.**
11:43:28 Q. **Please turn to PDX6.3. If you could just briefly**
11:43:36 **describe your experience at the PTO as an examiner?**
11:43:40 A. **Well, in 1988, I was a junior examiner in the biotech**

11:43:46 group. And then in 1991 I was promoted to primary examiner.
11:43:52 To become a primary examiner your office actions are
11:43:57 evaluated by senior people within your group, SPEs and the
11:44:02 group director, because they are evaluated on a very special
11:44:06 program, and then if you pass that program, you are granted
11:44:11 full signatory authority.
11:44:13 That's what I did. I passed the program.
11:44:16 Then in 1991, the very same year, my docket was
11:44:21 also evaluated by a special group down at the -- a special
11:44:25 board at the Commerce Department downtown. And they
11:44:29 determined that the applications in my docket required at
11:44:32 least a Master's degree in molecular biology. So I received
11:44:38 an examiner's senior level classification.
11:44:42 Then two years later in 1993, the same board
11:44:45 down at the Commerce Department again evaluated my docket
11:44:50 and determined that it required a Ph.D. in molecular biology
11:44:54 to examine those applications. So I was then classified as
11:45:00 an examiner Ph.D. level. And that is the highest level of
11:45:06 classification that an examiner can receive.
11:45:09 Q. And what was your experience as an administrative
11:45:13 patent judge?
11:45:14 A. Well, initially, I was an ex parte judge. And I sat
11:45:19 on three-judge panels. And we reviewed the examiners'
11:45:27 decisions, the examiners' office actions, the examiners'
11:45:32 decisions on patentability. And my decisions of those

11:45:36 **applications were the final agency decision.**

11:45:41 Q. **As an examiner in the biotechnology group, what roles**

11:45:44 **did you hold?**

11:45:46 A. **Well, as an examiner, I reviewed and evaluated the**

11:45:52 **patent applications that were before me, and I had to search**

11:45:57 **the prior published literature and patents to determine what**

11:46:04 **was known in the prior art at the time an application was**

11:46:08 **filed. And I prepared office actions and conducted**

11:46:12 **interviews with applicants' attorneys, and I, of course,**

11:46:19 **reviewed applicants' responses to my office actions and any**

11:46:23 **evidence that accompanied those responses.**

11:46:26 Q. **Did you receive any training as an examiner?**

11:46:29 A. **Yes. I received training both in the classroom and on**

11:46:33 **the job in the patent statutes, in the examination procedure**

11:46:38 **as set forth in the Code of Federal Regulations and the**

11:46:42 **Manual of Patent Examining Procedure.**

11:46:47 **So I evaluated the applications that came before**

11:46:50 **me based on those statutes and those regulations, and that**

11:46:58 **would include, you know, 35 U.S.C. 101, 102, 103 and 112.**

11:47:04 Q. **Did you ever receive any awards for your work as an**

11:47:07 **examiner?**

11:47:07 A. **Yes. In 1994 under the recommendation of my group**

11:47:15 **director I received the AIPLA Examiner of the Year Award.**

11:47:18 Q. **You mentioned that you were promoted to an APJ. Why**

11:47:21 **were you promoted?**

11:47:22 A. **I was promoted based on my ability to examine biotechnology applications. And I was the first APJ to go to the board that actually had a biotechnology background.**

11:47:37 Q. **What were your initial responsibilities as an APJ at the U.S. PTO?**

11:47:42 A. **Initially, I examined ex parte appeals from the examining board and rendered decisions on patentability. And those decisions were the final agency decision.**

11:47:57 Q. **Did you hear any other types of cases as an APJ?**

11:48:01 A. **Yes. I also conducted interference proceedings. And those decisions that I rendered covered the issues of patentability as well as priority. Those were also the final agency decision.**

11:48:18 Q. **How long were you an APJ?**

11:48:21 A. **Over 11 years.**

11:48:22 Q. **How many decisions, approximately, did you author?**

11:48:24 A. **Well, I authored over 250 ex parte decisions and 50 inter partes decisions. But I participated in approximately three times that many as Judge No. 2 and No. 3.**

11:48:42 **MR. HAUG: At this point plaintiffs offer Dr. Ellis as an expert witness in the practices and procedure before the U.S. PTO relating to the prosecution of patents during the time she was working for the U.S. PTO.**

11:48:55 **THE COURT: I would like to see counsel at sidebar.**

11:48:57

(The following took place at sidebar.)

11:57:12 THE COURT: Why do I need to hear from this witness?

11:57:12 MR. HAUG: Well, she is only -- I would only ask her two points.

11:57:12 THE COURT: I want to know why I need to hear from her.

11:57:12 MR. HAUG: Only if you think it would be helpful to you.

11:57:12 THE COURT: Well, if you think it would be helpful to your case. And why this is relevant. I have never heard this kind testimony before, Mr. Blumenfeld may correct me, he is probably over there -- I shouldn't say never. I probably have never permitted a patent examiner to testify as an expert in my courtroom. I want to know why I should make an exception today.

11:57:13 MR. HAUG: Only because of the issues that are in this case, particularly the laches issue and how the Patent Office deals with issues.

11:57:13 THE COURT: How is she going to help me understand the laches issue?

11:57:13 MR. HAUG: Your Honor, if you don't think you need it...

11:57:13 THE COURT: You are not going to put it on me. You have to make your record. If I am not going to let her

11:57:13 testify, which I am unlikely to, you have got to tell me why.

11:57:13 MR. HAUG: Ms. Ellis was in the PTO for a good 20 years, whatever, in the very same biotechnology group, 180, which prosecuted this particular patent at issue here. She is prepared to talk about the rules that were in force during that period of time, and also the Patent Office's policy on giving warning of laches.

11:57:14 THE COURT: What is your reaction to this?

11:57:14 MR. WIESEN: Your Honor, I don't think it's necessary. I think it's mainly legal testimony, talking about the Guidelines in the MPEP. They are more than welcome to cite them and argue from them. But I don't think a witness is necessary to describe them in this courtroom.

11:57:14 THE COURT: Why aren't the Guidelines, the citation to the MPEP sufficient.

11:57:14 MR. HAUG: If I can argue without this witness putting any of -- talking about any of them, if I can argue all those guidelines and MPEP sections and it is policies of the Patent Office with respect to laches, then I think that is sufficient, if Your Honor doesn't think --

11:57:14 THE COURT: What is your reaction to that?

11:57:14 MR. WIESEN: The Guidelines are published in the C.F.R., in the Federal Register. I think it's akin to citing a statute. I think the MPEP is often treated the

11:57:14 same way and cited as regulatory guidance. I don't think we
11:57:14 would object if that is what the issue is, just to put them
11:57:14 into the record.
11:57:14 THE COURT: Are you offering this testimony as
11:57:14 relevant to the prosecution practice, you said a couple of
11:57:14 times, with regard to prosecution laches, their practice is
11:57:14 somehow relevant to my decision in this case? If so, how?
11:57:14 MR. HAUG: Because the examiners are trained to
11:57:14 look for laches. If they find anything that is a laches
11:57:15 issue, they issue a warning. And no such warning was issued
11:57:15 in this case.
11:57:15 THE COURT: I should infer from that -- maybe
11:57:15 they missed it. No?
11:57:15 MR. HAUG: Your Honor will make that decision.
11:57:15 THE COURT: She is here. I am going to let her
11:57:15 testify. I doubt that I am going to consider the testimony.
11:57:15 You paid her. Let her go ahead and testify.
11:57:15 (End of sidebar conference.)
11:57:15 MR. HAUG: Your Honor, I think where I got to
11:57:15 is I offered Dr. Ellis as an expert.
11:57:15 MR. WIESEN: No objection, Your Honor.
11:57:15 THE COURT: She is accepted as an expert.
11:57:15 MR. HAUG: Thank you, Your Honor.
11:57:15 BY MR. HAUG:
11:57:15 Q. If we could turn to PDX6.5, please.

11:57:15 **Is this a summary of your opinions?**

11:57:15 A. **Yes, it is.**

11:57:15 Q. **Could you just please go through them quickly?**

11:57:15 A. **Yes. During the time of the '333 patent prosecution, the U.S. PTO could have issued a warning of prosecution laches, but it did not.**

11:57:15 **During the time of the '333 patent prosecution,**

11:57:16 **the 1988 MPEP Utility Guidelines that were set forth in 608.01(p) permitted use of in vivo or in vitro data or a combination thereof as proof of utility.**

11:57:16 **And that the '333 patent applicants complied with the 1995 U.S. PTO Utility Guidelines to rebut the rejection for lack of utility.**

11:57:16 Q. **You mentioned the issuance of a warning of prosecution laches. What do you mean by warning of prosecution laches?**

11:57:16 A. **Based on a board decision, patent examiners were instructed to issue a warning that a patent applicant would forfeit his or her patent rights if they filed continuation after continuation on allowed claims.**

11:57:16 Q. **I would like to turn to your second opinion. If you could please go to PDX-6.28.**

11:57:16 A. **Yes.**

11:57:16 Q. **At the time of the -- withdrawn.**

11:57:16 **What is MPEP 608.01(p)?**

11:57:16 A. **What is being shown here is the section of the MPEP**

11:57:16 that was in effect at the time the '333 patent applications were being prosecuted.

Q. Was this section in force from 1990 to 1997?

A. Well, it was in force. But this section was updated in 1995. So it became -- so that it made it very clear that the utility guidelines were directed to inventions involving biotech and immunotherapy.

Q. If you could turn to PDX-6.30, what do you mean by "proposed utility guidelines"?

A. Well, in 1995, because there was a lot of uproar in the biotech industry about all of the utility rejections that were being made in the biotech group, the Patent Office decided to write new utility guidelines for the examiners. And that was done in 1993, the first draft came out, and it was published in the Federal Register, as you see here, on January 3rd, 1995, at the same time it was also published in the MPEP.

MR. HAUG: No further questions, Your Honor.

THE COURT: Mr. Wiesen.

MR. WIESEN: No questions, Your Honor.

THE COURT: Thank you, Doctor. Please be careful stepping down.

(Witness excused.)

MR. HAUG: With that, Your Honor, plaintiffs rest.

11:57:17 **THE COURT: Mr. Wiesen.**

11:57:17 **MR. WIESEN: Your Honor, we have a very short video designation from Ms. Andresen, and then one live witness, Dr. Pines, who had been on our witness list. We have decided not to call him. We will just have Mr. Hofmann on commercial success.**

11:57:17 **THE COURT: Let's take a stretch.**

11:57:17 **(Recess taken.)**

12:08:49 **THE COURT: Please continue. Mr. Wiesen.**

12:08:51 **MR. WIESEN: Your Honor, defendant's rebuttal case will be brief. The first witness is Dr. Andresen, who is in the Global Medical Affairs Department at Shire. The designations are about nine minutes long.**

12:09:01 **THE COURT: Okay.**

12:09:06 **MR. WIESEN: We have transcripts to hand up.**

12:09:07 **THE COURT: Great. Okay.**

12:09:25 **(Designations played as follows.)**

12:09:27 **"Mr. Stull: So I will go ahead and mark as Exhibit 1, Fresenius notice of 30(b)(6) deposition of plaintiffs.**

12:09:39 **"And if you could look at Topic No. 21. Do you see that?**

12:09:45 **"Answer: Yes.**

12:09:45 **"Question: Is this one of the topics you understand you will be here to testify about?**

12:09:50 "Answer: Yes.

12:09:51 "Question: So if you could look at Topic 23, is
12:09:57 that another one of the topics you understand you are here
12:10:00 to testify about?

12:10:01 "Answer: Yes.

12:10:02 "Question: Okay. And how many products for HAE
12:10:07 does Shire have now?

12:10:09 "Answer: Are you talking about -- asking about
12:10:12 U.S. or --

12:10:13 "Question: How about U.S.?

12:10:14 "Answer: I think three.

12:10:17 "Question: Three?

12:10:18 "Answer: Yes.

12:10:19 "Question: Would that be Cinryze, Firazyr, and
12:10:24 Kalbitor?

12:10:24 "Answer: Yes.

12:10:25 "Question: Do they have a product in Phase III
12:10:27 trials for HAE?

12:10:28 "Answer: Yes.

12:10:28 "Question: Was that acquired from Dyax?

12:10:33 "Answer: Yes.

12:10:34 "Question: And when Firazyr was originally
12:10:37 approved in the U.S., it was approved for
12:10:39 self-administration. Correct?

12:10:43 "Answer: That's my understanding, yes.

12:10:44 "Question: At the time in 2011, are you aware
12:10:47 that Shire had any other products that were -- it was
12:10:51 marketing for HAE?
12:10:52 "Answer: I'm not aware of.
12:10:56 "Mr. Stull: Mark as Exhibit 11 a document with
12:11:00 Bates Nos. SHRSAN00436603 through 436854.
12:11:16 "And is this a copy of Shire's 10-K for the
12:11:19 fiscal year ending December 31, 2015?
12:11:23 "Answer: That's correct.
12:11:24 "Question: Would you turn to Page 22. Do you
12:11:27 see where there is a heading that says Recently Acquired
12:11:30 Product?
12:11:32 "Answer: Yes.
12:11:33 "Question: And below that there is a listing
12:11:35 for Kalbitor?
12:11:38 "Answer: Yes.
12:11:39 "Question: And above Kalbitor it says,
12:11:44 'Following completion of acquisition of Dyax on January 22,
12:11:49 2016. Shire obtained Kalbitor.'
12:11:54 "Is that correct?
12:11:55 "Answer: This is what is stated here, yes.
12:11:57 "Question: Mark as Exhibit 16 a document with
12:12:00 Bates Nos. SHRSAN0005127 through 5135.
12:12:12 "Does this appear to be a Shire document
12:12:15 regarding pre-approval key messages Q&A for Firazyr?

12:12:21 **"Answer: Yes.**

12:12:21 **"Question: So the question says, 'Is there a**
12:12:25 **medical need for Firazyr in the U.S. since there are several**
12:12:28 **other treatments already available to treat HAE?'**

12:12:35 **"Do you see that?**

12:12:36 **"Answer: I see that question.**

12:12:37 **"Question: Is that an accurate description of**
12:12:41 **the unmet need?**

12:12:44 **"Answer: In general, yes.**

12:12:48 **"Question: If you could turn to Page 8. Do you**
12:13:34 **see there is a question that states, 'How does**
12:13:41 **Firazyr/icatibant injection differ from existing therapies?'**

12:13:46 **"Answer: I see that question.**

12:13:47 **"Question: Is that an accurate description of**
12:13:49 **how Firazyr differs from existing therapies?**

12:13:52 **"Answer: Yes.**

12:14:03 **"Question: Has Shire marketed Firazyr in the**
12:14:06 **United States as being -- having superior efficacy in**
12:14:09 **treating acute attacks of HAE as compared to any of the**
12:14:13 **other known treatments for acute attacks of HAE?**

12:14:16 **"Answer: We have never shown superiority. This**
12:14:20 **would mean a head-to-head study.**

12:14:24 **"Question: And has there ever been a**
12:14:29 **head-to-head study?**

12:14:30 **"Answer: No, never.**

12:14:32 "Mr. Stull: I will mark as Exhibit 17 a document with Bates numbers SHRSAN00005688 through 5704.

12:14:50 "Is this a Shire presentation entitled Firazyr Launch Commercial Team Q&A?

12:14:58 "Answer: This is what it says.

12:14:59 "Question: Is this something that would have been generated from the marketing department?

12:15:05 "Answer: As it is commercial team, yes, I would assume it is.

12:15:10 "Question: And if you could look to what is Page 3 of the presentation, there is a question at the top which says, 'How does the efficacy or safety of Firazyr compare to other HAE treatments?'

12:15:32 "Answer: I see that.

12:15:33 "Question: And there's a response. There's two bullet points.

12:15:38 "Do you see that?

12:15:39 "Answer: Yes.

12:15:39 "Question: Is that response accurate?

12:15:43 "Answer: Yeah. The first one, I said already, there have never been any head-to-head studies; and the second, yes.

12:15:52 "Question: And the second one is -- just refers to the individual product prescribing information?

12:15:58 "Answer: Yes.

12:15:59 "Mr. Stull: Mark as Exhibit 19 a document with
12:16:04 Bates Nos. SHRS00439330 through 439389.
12:16:14 "Does this appear to be a Shire presentation
12:16:16 entitled 2013 Firazyr Global Medical Affairs Plan dated
12:16:21 August 2012?
12:16:24 "Answer: That's correct.
12:16:25 "Question: And if you could look at Page 8 of
12:16:28 the presentation, do you see there's a -- it's sort of a
12:16:43 flowchart on the right-hand side that says Operating
12:16:47 Strategies, and there are four operating strategies. Is
12:16:52 that correct?
12:16:53 "Answer: Yes.
12:16:53 "Question: Do you see the first one says,
12:16:56 'Disseminate scientific data of Firazyr as preferred
12:17:00 first-line treatment for all HAE attacks (unique MoA, key
12:17:10 indicator, key mediator, efficacy).'
12:17:16 "Do you see that?
12:17:18 "Answer: Yes.
12:17:18 "Question: What does preferred first-line
12:17:21 treatment mean there?
12:17:22 "Answer: Because of the entity icatibant it has
12:17:27 several aspects which are unique, as like the mode of
12:17:36 action, that it is targeted to the bradykinin receptors,
12:17:46 what hasn't been on the market so far, and it is directly
12:17:50 targeting the key mediator bradykinin.

12:17:54 **"Question: There is no study that's shown that**
12:17:56 **the unique method of action leads to superior efficacy.**
12:18:00 **Right?**
12:18:00 **"Answer: That's right.**
12:18:01 **"Question: Back in 2011, Kalbitor is not**
12:18:05 **approved for self-administration; is that correct?**
12:18:09 **"Answer: Yes.**
12:18:09 **"Question: And what -- do you know why it**
12:18:12 **wasn't approved for self-administration?**
12:18:14 **"Answer: Like for performing, and they had**
12:18:17 **anaphylactic reaction in the study of some cases; and,**
12:18:21 **therefore, it can't be done and can't just be provided by a**
12:18:24 **healthcare provider.**
12:18:28 **"Question: Because of the anaphylactic shock?**
12:18:30 **"Answer: Yeah. You can never exclude that.**
12:18:32 **"Question: Does Shire market its product as**
12:18:34 **having a superior safety profile as to the other products**
12:18:38 **that are marketed for treatment of acute attacks of HAE?**
12:18:43 **"Answer: It's difficult to judge, because we**
12:18:45 **have not done head-to-head safety studies.**
12:18:47 **"Question: So do they market it based on**
12:18:50 **superior safety to the other acute HAE products?**
12:18:56 **"Answer: No."**
12:19:06 **THE COURT: Mr. Wiesen, how long will this next**
12:19:09 **witness take, approximately?**

12:19:10 **MR. WIESEN: I believe the direct examination is**
12:19:13 **maybe a half-hour or less.**
12:19:15 **THE COURT: Let's start with the witness and**
12:19:19 **see.**
12:19:20 **MR. WIESEN: Your Honor, defendants call Mr.**
12:19:22 **Ivan Hofmann, and Mr. Sherry will conduct the examination.**
12:19:25 **THE COURT: Okay.**
12:19:42 **... IVAN HOFMANN, been duly sworn as a witness,**
12:19:50 **was examined and testified as follows ...**
12:19:54 **THE COURT: Good morning, Mr. Hofmann.**
12:20:00 **THE WITNESS: Good morning, Your Honor.**
12:20:02 **THE COURT: I should say afternoon.**
12:20:02 **THE WITNESS: I guess so. You are right.**
12:20:07 **DIRECT EXAMINATION**
12:20:07 **BY MR. SHERRY:**
12:20:08 Q. **Mr. Hofmann, where are you currently employed?**
12:20:24 A. **I am a vice president and managing director at Gleason**
12:20:29 **IP, which is an economic accounting and financial consulting**
12:20:32 **firm where I am the leader of the intellectual property**
12:20:34 **practice.**
12:20:34 Q. **And what is the nature of your work in the economics**
12:20:39 **of the pharmaceutical industry?**
12:20:40 A. **So sometimes I am called upon to analyze economic**
12:20:43 **issues involving intellectual property in a dispute setting**
12:20:47 **such as this, analyzing issues like secondary considerations**

12:20:51 of nonobviousness as well as damages, irreparable harm.
12:20:54 Outside of a dispute setting, I regularly
12:20:57 analyze the economics of intellectual property for things
12:20:59 like licensing, product pipeline consulting, market
12:21:04 analysis, et cetera.
12:21:04 Q. How many pharmaceutical products have you performed
12:21:08 economic analysis on?
12:21:09 A. Over the last 20 years, more than a hundred different
12:21:13 pharmaceutical products, including virtually every major
12:21:17 therapeutic class of drugs.
12:21:18 Q. Please turn to DTX-314 in your binder. What is this
12:21:26 document?
12:21:26 A. It is a copy of my curriculum vitae.
12:21:29 Q. Is it up to date and accurate?
12:21:31 A. It is.
12:21:34 MR. SHERRY: We present Mr. Hofmann as an expert
12:21:36 in the field of pharmaceutical economics.
12:21:38 THE COURT: Mr. Blumenfeld?
12:21:40 MR. BLUMENFELD: No objection, Your Honor.
12:21:41 THE COURT: The witness is accepted as an expert
12:21:43 in the field.
12:21:44 BY MR. SHERRY:
12:21:44 Q. Mr. Hofmann, what did Fresenius ask you to do in this
12:21:47 matter?
12:21:47 A. I was asked to respond to certain issues involving

12:21:50 **pharmaceutical economics, specifically, to respond to some**
12:21:53 **of the opinions expressed by Dr. Bell regarding commercial**
12:21:57 **success and nexus with respect to Claim 14 of the '333**
12:22:02 **patent.**
12:22:02 Q. **Have you prepared slides to assist you in presenting**
12:22:06 **your opinions today?**
12:22:10 A. **I have.**
12:22:11 Q. **Can you briefly summarize your opinions regarding**
12:22:14 **plaintiffs' claims of commercial success?**
12:22:16 A. **Sure. The primary focus of my testimony is the lack**
12:22:19 **of nexus between the commercial performance of Firazyr and**
12:22:24 **Claim 14 of the '333 patent. And there is three main areas.**
12:22:29 **The first is Dr. Bell only compared the**
12:22:31 **performance of Firazyr to other marketed products. He**
12:22:36 **didn't compare the performance of Firazyr versus the closest**
12:22:41 **prior art and failed to show a nexus because of that.**
12:22:45 **Secondly, there are unique aspects of the small**
12:22:48 **Orphan Drug market for Firazyr as a treatment of HAE,**
12:22:54 **combined with certain business strategies of Shire, that**
12:22:58 **have nothing to do with the '333 patent that explain the**
12:23:01 **performance of Firazyr.**
12:23:03 **And then finally, we have some real-world**
12:23:05 **objective evidence of the failure of Hoechst to do anything**
12:23:10 **commercially with icatibant despite having the patent and**
12:23:16 **the resources for a dozen years to the compound.**

12:23:20 Q. **Let's turn to your opinions in a little bit more**
12:23:22 **detail.**
12:23:24 **Could you please explain how the commercial**
12:23:26 **performance of Firazyr is attributable to features known in**
12:23:29 **the prior art?**
12:23:30 A. **Sure. I think we already heard some testimony this**
12:23:32 **week that subcutaneous injection through self-administration**
12:23:38 **and portability are really the drivers of the performance of**
12:23:41 **Firazyr. And my understanding is that the convenience**
12:23:44 **associated with subcutaneous injection are properties that**
12:23:49 **are shared with other bradykinin antagonists and were known**
12:23:53 **in the prior art. As a result, there is a failure to show**
12:23:57 **nexus because these attributes which drive the performance**
12:24:00 **of Firazyr were known in the prior art.**
12:24:02 Q. **What led you to the conclusion that**
12:24:05 **self-administration is a convenience that drives Firazyr's**
12:24:11 **market performance?**
12:24:11 A. **A combination of Shire documents, as well as**
12:24:14 **third-party discussion, and then I think we heard that from**
12:24:17 **Dr. Kaplan and even Dr. Bell.**
12:24:19 Q. **Let's look at the Shire documents. Can you please**
12:24:24 **turn to JTX-43 in your binder, Page 32, which we have up on**
12:24:31 **the screen here. Can you tell us what document this is?**
12:24:33 A. **Yes. This is a 2017 HAE strategic business plan. And**
12:24:38 **this is a slide from within that document.**

12:24:40 Q. **And what does Shire's business plan say about the**
12:24:50 **importance of portability and self-administration by**
12:24:52 **subcutaneous injection?**
12:24:53 A. **I have highlighted that on the screen. Basically,**
12:24:55 **portability and self-administration are key attributes that**
12:24:58 **drive prescribing.**
12:24:58 Q. **Let's turn to the second part of your opinion. If you**
12:25:02 **go back to the previous slide. If you turn to Slide 9, Mr.**
12:25:08 **Chase.**
12:25:10 **What did you do to reach a conclusion regarding**
12:25:13 **whether the properties of icatibant that allow**
12:25:19 **self-administration are found in the prior art?**
12:25:21 A. **I am not a scientist so I relied on Dr. Bachovchin's**
12:25:25 **opinions in that case.**
12:25:26 Q. **What information from Dr. Bachovchin regarding the**
12:25:28 **properties of icatibant did you use in your analysis?**
12:25:30 A. **So I have summarized some of his testimony from**
12:25:33 **earlier this week on the screen. But basically, it's his**
12:25:37 **opinion and my understanding that these attributes of the**
12:25:41 **ability for subcutaneous objection --**
12:25:46 **THE COURT: You might want to direct your**
12:25:47 **attention out there. I am listening.**
12:25:50 **THE WITNESS: Of course, Your Honor. Excellent.**
12:25:52 **The attributes that allow for subcutaneous**
12:25:55 **injection and tolerability and stability are attributes that**

12:25:58 **were known and attributes contained in prior bradykinin**
12:26:04 **antagonists.**
12:26:05 **BY MR. SHERRY:**
12:26:05 Q. **How did this scientific information regarding**
12:26:08 **icatibant in the prior art affect your economic analysis?**
12:26:12 A. **Well, my understanding from an economic perspective is**
12:26:15 **that in order to show nexus one has to show that there are**
12:26:19 **incremental novel properties over what was known in the**
12:26:23 **prior art, and that that has not been shown in the analysis**
12:26:28 **we heard from Dr. Bell.**
12:26:31 Q. **Thank you, Mr. Hofmann.**
12:26:34 **Can you explain, let's turn to your next**
12:26:37 **opinion, can you explain your opinions regarding the HAE**
12:26:40 **market and Shire's business strategies?**
12:26:43 A. **Sure. There are several attributes to this. As I**
12:26:48 **have touched on earlier, HAE is a very small market. It's**
12:26:52 **an Orphan Drug. And because it's a very small market, there**
12:26:56 **are unique attributes with respect to pricing and**
12:26:58 **reimbursement.**
12:27:00 **There have also been a number of business**
12:27:02 **strategies undertaken by Shire which have allowed them to**
12:27:07 **aggressively take advantage of these market dynamics. And**
12:27:11 **consistent with that, Shire has also acquired a number of**
12:27:14 **HAE products which gives them some control and a leadership**
12:27:17 **position in the marketplace that again affects the**

commercial performance of Firazyr.

Q. Well, let's start by talking about the size of the market for Firazyr. You mentioned that HAE is a rare disease. How uncommon does a disease need to be in order to be considered rare?

A. Well, it is an Orphan Drug. My understanding in the U.S., that means a prevalence of 200,000 or less individuals in the U.S.

Q. How does the HAE market compare with the market for other rare diseases?

A. It is kind of an ultra-Orphan Drug. We are talking about thousands of individuals in terms of prevalence, versus that 200,000 threshold, which is already low.

Q. How does the size of a patient population typically affect drug prices?

A. So patients typically don't pay out of pocket for the actual cost of the drug. They rely on third-party payors like insurance companies.

So it isn't a traditional kind of supply and demand dynamic for pharmaceutical products. Typically, these insurance companies will negotiate pricing with the manufacturers, and for diseases with high prevalence, like diabetes, they can exert some influence and focus a lot of attention on trying to get rebates and discounts, whereas for small populations, for Orphan Drugs, there is less

12:28:41 attention devoted.
12:28:41 Q. And how are drug prices affected when the patient
12:28:47 population is very small?
12:28:50 A. So because there is only a few thousand people that
12:28:53 are actually undergoing treatment for HAE, and there are
12:28:56 several thousand third-party payors or insurance companies
12:29:00 in the country, any particular payor only has a handful of
12:29:06 patients that may be treated for HAE. So they typically
12:29:09 devote much less resources to something like an ultra-Orphan
12:29:15 Drug like HAE, which allows the manufacturer to basically
12:29:17 charge much higher prices per patient.
12:29:19 Q. Does Shire acknowledge that the market for Firazyr has
12:29:25 this dynamic with third-party payors?
12:29:29 A. Yes, that was in the Shire documents, business plans,
12:29:32 et cetera.
12:29:32 Q. Please turn to JTX-12 in your binder, which we have up
12:29:36 on the screen now, Page 25. Can you tell us what document
12:29:40 this is?
12:29:41 A. Yes. This is a business plan from 2015.
12:29:44 Q. What does the Shire business plan say about the HAE
12:29:47 market?
12:29:47 A. Well, I have highlighted an excerpt of it. It says,
12:29:51 Payors report that HAE is a low priority to manage.
12:29:53 You can see the title is HAE Continues to Fly
12:29:56 Under the Radar. This is consistent with what I was saying,

12:29:59 **that payors don't really focus as much attention on pricing**
12:30:03 **for ultra-Orphan Drugs like for HAE.**
12:30:06 Q. **Let's take a look at another aspect of the HAE market.**
12:30:10 **In developing your opinions, did you find information**
12:30:14 **regarding how frequently Firazyr is used by patients who are**
12:30:17 **prescribed the drug?**
12:30:18 A. **I did.**
12:30:18 Q. **Would you please turn to DTX-298, the last page, Page**
12:30:25 **56. We have it up on the screen. Can you explain what this**
12:30:30 **slide shows?**
12:30:31 A. **Yes. This is a slide from the 2016 long-range**
12:30:36 **planning for HAE by Shire.**
12:30:38 **This is kind of a busy dual-axis graph. So I**
12:30:41 **will walk through what it tells us, because it's rather**
12:30:44 **important and telling.**
12:30:46 **What you have on the bottom is quintiles. And**
12:30:49 **what quintiles means is basically Shire is looking at of the**
12:30:53 **uses of Firazyr how does it break out by patient population.**
12:30:57 **20 percent of sales is represented in each quintile.**
12:31:01 **On the left side of the dual-axis graph, it's**
12:31:07 **the percentage of Firazyr users in that year. And that's**
12:31:10 **what's covered by these bars.**
12:31:12 **So you can see the top quintile, the 20 percent**
12:31:16 **of uses is actually one percent of patients consumed 20**
12:31:22 **percent of Firazyr. And you can see like the bottom**

12:31:26 quintile, 68 percent of patients or 69 percent, you know,
12:31:30 cover that 20 percent.
12:31:31 So you have high users with a concentrated use
12:31:34 of Firazyr.
12:31:36 Then what's on the right side of the dual-axis
12:31:38 graph is the average number of syringes per patient. And
12:31:44 that's what's covered in the line graph. You can see for
12:31:47 the high users, they are using about 30 syringes a month,
12:31:53 which then declines as you go to lower average users.
12:31:56 Q. And what does DTX-298 show regarding Firazyr usage
12:32:08 patients?
12:32:08 A. You can see that the title is Five Percent of Patients
12:32:12 Account For 40 Percent of Firazyr Users. And they have
12:32:16 highlighted that. You can see that these top two quintiles
12:32:20 represent a very high concentration, represented a very
12:32:23 limited number of patients representing a significant
12:32:25 portion of Firazyr sales.
12:32:27 Q. Now, five percent of patients account for 40 percent
12:32:31 of sales, how many patients are we actually talking about
12:32:34 here?
12:32:34 A. Right. So five percent of patients, based on some of
12:32:37 the patient information, we are talking about less than a
12:32:40 hundred patients. If you look at the top quintile, that one
12:32:44 percent, you know, these 16 or less than 20 patients who are
12:32:48 using 30 syringes a month are actually consuming millions of

12:32:55 dollars worth of Firazyr per patient. I think we heard that
12:32:59 Firazyr costs about nine to ten thousand per syringe.
12:33:03 Because they are using 30 syringes a month, it is about more
12:33:06 than three million dollars per patient in that group.
12:33:08 Q. How does the size of the HAE market and Firazyr's
12:33:15 usage patterns affect your economic analysis of commercial
12:33:18 success?
12:33:18 A. Well, these are economic and market dynamics that
12:33:22 really have nothing to do with the patent. They are
12:33:24 commercial business things that drive the dollar sales we
12:33:27 heard about that are unrelated to the patent.
12:33:30 Q. Let's turn to Shire's business strategy regarding
12:33:37 pricing. Please turn to PTX-092, which we have a
12:33:45 representation of that up on the screen. This was
12:33:49 information discussed in Dr. Bell's testimony.
12:33:52 Can you explain what this graph shows about how
12:33:55 the price of Firazyr varied over time as compared to
12:34:00 competing acute HAE therapies?
12:34:02 A. Sure. So all of these therapies are very expensive
12:34:05 per attack, as I just explained. But Shire has deployed a
12:34:10 commercial strategy where they have consistently kept the
12:34:13 price of Firazyr about one to three thousand dollars below
12:34:17 the cost of other available treatments for acute attacks, as
12:34:23 a kind of business strategy.
12:34:24 Q. How does this discounted pricing affect your analysis

12:34:28 of commercial success?
12:34:29 A. Well, this is yet another commercial and business
12:34:34 strategy that is unrelated to the '333 patent that drives
12:34:36 some of the sales and volume of Firazyr.
12:34:38 Q. Let's turn to the next aspect of your opinion,
12:34:44 regarding Shire's business strategy, the position in the
12:34:52 market. What is the perception of Shire in the HAE market?
12:34:54 A. Well, they have through acquisition, you know, become
12:34:57 a leader in the space, having control of a number of
12:34:59 treatments for HAE.
12:35:00 Q. And which products do they control?
12:35:04 A. They have Firazyr, Cinryze and Kalbitor, which are
12:35:07 three out of the five products available for the treatment
12:35:10 of HAE.
12:35:10 Q. And why does Shire's leadership position in the market
12:35:14 matter?
12:35:14 A. Well, for a few commercial reasons. One, it allows
12:35:17 them to manage the marketing attention and resources devoted
12:35:21 to the different products. It also allows them to exert
12:35:26 some influence over pricing strategy. So it's that
12:35:30 combination of commercial strategies which, again, drives
12:35:34 sales but really has nothing to do with the patent.
12:35:36 Q. And how does Shire's leadership position affect the
12:35:41 commercial success analysis?
12:35:43 A. Well, alongside some of the things I already talked

12:35:45 about, this is another business and commercial strategy
12:35:48 unrelated to the '333 patent that explains the performance
12:35:51 of Firazyr.
12:35:52 Q. Let's turn to the next point on nexus, which concerns
12:35:58 the gap between the invention of icatibant and the
12:36:02 development of the HAE indication. How does the sequence of
12:36:06 events in the development of icatibant affect your economic
12:36:10 analysis?
12:36:11 A. Well, what we have is we have some real-world evidence
12:36:15 where Hoechst created the icatibant molecule, worked on it
12:36:20 for many years, and then essentially abandoned the compound.
12:36:24 And this provides evidence that something other than the
12:36:27 compound that later occurred explains the performance of
12:36:31 Firazyr.
12:36:31 Q. Before we just get into the economic implications,
12:36:35 let's just go over the timeline. Can you give an overview
12:36:40 of the period that ultimately resulted in Firazyr's
12:36:44 commercial product?
12:36:45 A. Sure. On the far left, we have the brief period of
12:36:47 development of icatibant in the '87-'88 time frame. Then in
12:36:54 gray, we have the period where Hoechst worked on finding
12:36:58 uses for icatibant and ultimately abandoned development of
12:37:02 the product. In green, we have a period of time where
12:37:06 Jerini out-licensed the compound and did work on cirrhosis
12:37:12 and HAE. And then finally, in the last orange period, we

12:37:17 **have the, 20 years later, commercial sales of Firazyr.**

12:37:21 Q. **So when did Hoechst first develop icatibant?**

12:37:26 A. **That's in 1989.**

12:37:28 Q. **When did work begin on developing a method of using**

12:37:32 **icatibant to treat HAE?**

12:37:35 A. **Not until after 2001 when Jerini took over and worked**

12:37:41 **on cirrhosis and HAE.**

12:37:43 Q. **And what happened during the 12-year period in between**

12:37:48 **the development of icatibant and the beginning of work on**

12:37:53 **developing a method and using that method of using icatibant**

12:37:56 **to treat HAE?**

12:37:57 A. **Well, Hoechst was focused on larger population**

12:38:02 **indications, things like rheumatoid arthritis and asthma and**

12:38:06 **rhinitis. They worked on those potential indications and**

12:38:09 **then ultimately gave up on development and abandoned the**

12:38:12 **compound.**

12:38:13 Q. **And did you identify information in preparing your**

12:38:18 **opinions for this case showing that Hoechst abandoned the**

12:38:22 **element of icatibant before it was licensed to Jerini?**

12:38:26 A. **I did. There was some testimony from Dr. Knolle that**

12:38:29 **I relied on.**

12:38:29 Q. **What was his testimony?**

12:38:31 A. **Well, I put it on the screen. I mean, basically, he**

12:38:35 **described icatibant as a dead compound sitting in the**

12:38:38 **basement at Hoechst. Basically after having worked on it**

12:38:41 **for more than a decade, the company discontinued development**
12:38:46 **and ultimately out-licensed the product to Jerini.**
12:38:49 Q. **And what do you conclude with respect to commercial**
12:38:54 **success from Hoechst's failure to exploit icatibant**
12:38:59 **commercially while they had it?**
12:39:00 A. **Well, the whole construct of commercial success is the**
12:39:05 **idea that there would have been motivation for others to**
12:39:08 **potentially exploit the invention, as an example, as shown**
12:39:14 **through commercial sales. But here we have Hoechst, a**
12:39:17 **worldwide pharmaceutical company that devoted 12 years of**
12:39:20 **time and resources and was unable to find a use, commercial**
12:39:24 **use for icatibant. This provides real-world evidence that**
12:39:30 **something other than the icatibant compound and the '333**
12:39:33 **patent explains the much later commercial performance of**
12:39:37 **Firazyr, things like the method of use for the treatment of**
12:39:40 **HAE, the particular formulation for subcutaneous injection,**
12:39:45 **et cetera.**
12:39:45 Q. **I would like to ask you a few questions about Dr.**
12:39:49 **Bell's analysis.**
12:39:50 **Did Dr. Bell apportion Firazyr's commercial**
12:39:54 **performance to factors other than the patents in suit?**
12:39:57 A. **No. He attributed everything to the '333 compound**
12:40:00 **patent.**
12:40:01 Q. **What factors should Dr. Bell have considered when**
12:40:04 **considering the marketplace performance of Firazyr?**

12:40:07 A. **As kind of illustrated by that timeline, there were later things like the method of use for the treatment of HAE and the formulation that allows for subcutaneous injection that he didn't ascribe any value to.**

12:40:19 **He also didn't address some of the business and commercial strategies I talked about, the unique aspects of the Orphan Drug market and the business strategies of Shire.**

12:40:28 Q. **And in your opinion, why is it important to ascribe value to the method of treating acute attacks of HAE with icatibant?**

12:40:37 A. **Well, it undermines his claims of nexus by ascribing all the commercial sales of Firazyr to the '333 patent. He fails to attribute the very important and later development of things like the method of use, the formulation, and the business strategies undertaken by Shire.**

12:40:58 Q. **Can I have Slide 22, please.**

12:41:03 **Mr. Hofmann, can you please briefly summarize your opinions?**

12:41:06 A. **Sure. So, as I said, the focus is the lack of nexus between the performance of Firazyr and the '333 patent. In particular, the performance and the ability to subcutaneously inject are things that I understand were known in the prior art.**

12:41:24 **There is the unique aspects of the Orphan Drug market and the business strategies of Shire that explain the**

12:41:29 **performance.**

12:41:30 **And then, really, very compelling is the actual**
12:41:34 **objective period that we have, where Hoechst tried and**
12:41:37 **failed to develop a commercial use for icatibant that shows**
12:41:40 **that something other than the molecule must explain the**
12:41:43 **commercial performance of Firazyr.**
12:41:45 Q. **Thank you, Mr. Hofmann. No further questions.**
12:41:48 **THE COURT: Mr. Blumenfeld.**
12:41:50 **MR. BLUMENFELD: Thank you, Your Honor.**
12:41:52 **CROSS-EXAMINATION**
12:41:52 **BY MR. BLUMENFELD:**
12:41:57 Q. **If I may hand up some notebooks, I hope I won't be**
12:42:00 **using many of these exhibits.**
12:42:25 **Good afternoon, Mr. Hofmann.**
12:42:27 A. **Good afternoon.**
12:42:28 Q. **We haven't met before. My name is Jack Blumenfeld.**
12:42:31 **Nice to meet you.**
12:42:33 A. **Nice to meet you as well.**
12:42:34 Q. **I just want to ask you a few questions this afternoon.**
12:42:37 **You talked about how there is a small Orphan**
12:42:40 **Drug market for hereditary angioedema.**
12:42:44 **Now, Firazyr is an Orphan Drug. Right?**
12:42:47 A. **It is.**
12:42:47 Q. **Berinert is an Orphan Drug?**
12:42:51 A. **It is.**

12:42:51 Q. **Kalbitor is an Orphan Drug?**

12:42:53 A. **Yes.**

12:42:54 Q. **And so this is the same small market for all three of**
12:42:58 **those Orphan Drugs. Right?**

12:43:00 A. **Yes. They are all approved for similar indications.**

12:43:03 Q. **You have looked at the relative market shares of those**
12:43:06 **products. Correct?**

12:43:08 A. **I have, yes.**

12:43:08 Q. **And could we put up PDX-4.6.**

12:43:24 **This PDX-4.6, this is one of Dr. Bell's slides.**
12:43:27 **You have seen the before. Right?**

12:43:29 A. **I have.**

12:43:30 Q. **You don't dispute any of the data that he put together**
12:43:37 **for this slide. Correct?**

12:43:38 A. **It does reflect the underlying data accurately. I**
12:43:43 **disagree with his conclusions on it. But, yes, I agree.**

12:43:46 Q. **Firazyr greatly outperformed Berinert and Kalbitor in**
12:43:51 **the HAE market. Correct?**

12:43:53 A. **I think for the reasons I explained on direct, that's**
12:43:55 **right.**

12:43:55 Q. **Now, one of the things you talked about was the**
12:43:59 **multiple products that Shire has. Right?**

12:44:01 A. **Correct.**

12:44:02 Q. **Now, from 2011 to 2013, Firazyr was Shire's only**
12:44:11 **product in the HAE market. Right?**

12:44:13 A. **Correct. The others were acquired later.**
12:44:15 Q. **They were acquired later?**
12:44:17 A. **Correct.**
12:44:17 Q. **Kalbitor really, right toward the end of the graph**
12:44:22 **that is shown here?**
12:44:23 A. **Correct, in 2016.**
12:44:25 Q. **And from 2011 to 2013, when Firazyr was Shire's only**
12:44:34 **product, it outperformed Berinert and Kalbitor by a lot of**
12:44:41 **dollars. Correct?**
12:44:42 A. **Well, I mean, the vast majority of the dollars come in**
12:44:46 **the period after they acquired Cinryze and had control of**
12:44:50 **both products. But I don't disagree that it outpaced the**
12:44:52 **other products in that period.**
12:44:54 Q. **You are in fact not contesting any of Dr. Bell's sales**
12:45:02 **and marketplace performance data. Is that correct?**
12:45:06 A. **In terms of data, I think that's right. I mean, I**
12:45:09 **don't think he adequately addressed the unique aspects of**
12:45:11 **the high prices for Orphan Drugs and the impact that has on**
12:45:15 **those dollars. But, yes, I would agree with you.**
12:45:18 Q. **Let's talk about that a little bit.**
12:45:22 **You referred during the course of your testimony**
12:45:26 **to document JTX-43. Can you turn to that?**
12:45:33 **It's in the book that Mr. Sherry gave you.**
12:45:42 A. **Okay.**
12:45:42 Q. **And you prepared a Slide, let me get the right slide,**

12:45:53 **pointing to Page 32 of this document. Right?**

12:45:59 **It's your slide, if you have it in front of you,**

12:46:02 **DDX6-7?**

12:46:04 A. **Yes.**

12:46:06 Q. **And what you pointed to on this page was "Portability**

12:46:13 **and self-administration are key Firazyr attributes that**

12:46:18 **drive prescribing."**

12:46:19 **Do you see that?**

12:46:20 A. **Yes.**

12:46:20 Q. **Above that, three bullet points above that, it says,**

12:46:25 **"70 percent of HCPs agreed patients should treat symptoms as**

12:46:31 **soon as they arise."**

12:46:34 **Right?**

12:46:34 A. **I do see that.**

12:46:35 Q. **And treating symptoms of HAE patients quickly is**

12:46:40 **important to the patients, isn't it?**

12:46:43 A. **I am not a clinician. But certainly, the subcutaneous**

12:46:47 **ready-to-use self-injection does contribute to that, yes.**

12:46:52 Q. **And that's one of the attributes of Firazyr. Right?**

12:46:56 A. **Yes.**

12:46:57 Q. **Now, can we turn back in this document to JTX-13.28.**

12:47:08 A. **I am sorry. Turn to what?**

12:47:10 Q. **I am sorry, 43.28. A few pages before the one you**

12:47:17 **were looking at.**

12:47:18 A. **All right.**

12:47:18 Q. **And on this page it says, "Payors recognize the burden**
12:47:23 **of HAE and importance of on-demand access; value of**
12:47:28 **prophylaxis varies."**
12:47:31 **Do you see that?**
12:47:31 A. **I do see that.**
12:47:32 Q. **On-demand access, that means at-home access, the**
12:47:37 **patients have it right there and they can use it?**
12:47:39 A. **Ready to use subcutaneous self-administration.**
12:47:42 Q. **That's important to patients. Right?**
12:47:44 A. **Correct.**
12:47:44 Q. **And important to doctors?**
12:47:46 A. **That's my understanding.**
12:47:47 Q. **And if you look down, there is a heading that says**
12:47:51 **"Value On-Demand," if we blow that up, this is talking about**
12:47:55 **payors, right, like insurance companies and other health**
12:47:59 **care payors?**
12:48:00 A. **Correct.**
12:48:01 Q. **"Payors care about onset and effectiveness of relief**
12:48:04 **and are also interested in effectiveness of a single**
12:48:09 **injection. They rate highly the ability for patients to**
12:48:12 **self-administer and value rapid initiation of treatment and**
12:48:17 **flexibility."**
12:48:18 **Do you see that?**
12:48:19 A. **I do.**
12:48:19 Q. **Those are things that payors do value. Correct?**

12:48:22 A. **Yes. And it goes on to talk about the low cost, which**
12:48:26 **I talked about. But, yes.**
12:48:27 Q. **You talked about the cost. You didn't talk about the**
12:48:30 **rest of this?**
12:48:31 A. **No, I did. I talked about the importance of**
12:48:33 **self-administration and subcutaneous injection.**
12:48:36 Q. **It also talks about payors care about onset and**
12:48:41 **effectiveness of relief and in addition the patient's**
12:48:48 **ability to self-administer. Right?**
12:48:50 A. **I see that.**
12:48:52 Q. **And another attribute of Firazyr is the effectiveness**
12:48:56 **of the relief that it provides to patients. Right?**
12:49:01 A. **Yeah, among other attributes, yes.**
12:49:03 Q. **And the effectiveness of relief that Firazyr provides**
12:49:07 **to patients, that is an attribute of icatibant. Correct?**
12:49:14 A. **Yeah. I would defer to technical experts on that. I**
12:49:17 **am not a medicinal chemist or formulator. But, you know,**
12:49:21 **that's part of it, sure.**
12:49:23 Q. **If there was no icatibant in the Firazyr, it wouldn't**
12:49:27 **treat the acute attacks. Correct?**
12:49:31 A. **Combined with the formulation and method of use, I**
12:49:36 **would agree with that.**
12:49:36 Q. **And Firazyr is the only FDA-approved treatment for**
12:49:42 **acute attacks of hereditary angioedema that is**
12:49:46 **self-administered subcutaneously. Right ?**

12:49:51 A. **That's my understanding.**

12:49:52 Q. **Can we put up your Slide 6-6.**

12:50:04 **This slide at the top, it refers to "Features Responsible for Firazyr's Performance."**

12:50:07 **Do you see that?**

12:50:10 A. **It goes on. But yes.**

12:50:11 Q. **Right. You talked about shared with known peptides.**

12:50:13 **But this slide is directed to features responsible for Firazyr's performance. Right?**

12:50:17 A. **That's the heading, yes.**

12:50:19 Q. **And then the third bullet point, you said, "Icatibant's convenience properties are shared with known bradykinin antagonist peptides."**

12:50:22 **Do you see that?**

12:50:23 A. **In reliance on Dr. Bachovchin, yes.**

12:50:29 Q. **Right. I understand you are relying on him.**

12:50:31 **When you were referring at the top of the slide to the features responsible for Firazyr's performance, and then at the bottom of the slide to icatibant's convenience properties, you were referring to the same thing. Right?**

12:50:34 A. **Essentially.**

12:50:34 Q. **And what you were saying is that the features responsible for Firazyr's performance were a result of icatibant's properties. Right?**

12:50:37 A. **Well, I mean, I think we heard from Dr. Andresen,**

12:50:40

12:50:42

12:50:47

12:50:51

12:50:57

12:50:58

12:51:01

12:51:07

12:51:09

12:51:14 **icatibant really doesn't differentiate on efficacy. What is**
12:51:18 **differentiated, as I explained, is the method of use through**
12:51:20 **subcutaneous self-injection. That is what I am talking**
12:51:23 **about here.**
12:51:24 Q. **It doesn't differentiate from what in terms of**
12:51:29 **efficacy?**
12:51:31 A. **Other available treatments.**
12:51:33 Q. **Now, there are no other available treatments that are**
12:51:38 **based on bradykinin antagonist peptides. Correct?**
12:51:44 A. **Commercially, I am not aware of any.**
12:51:46 Q. **Are you aware of any that are in development?**
12:51:51 A. **That's a better question for a technical expert.**
12:51:53 Q. **Now, the convenience properties that you talk about,**
12:52:00 **they include subcutaneous administration?**
12:52:02 A. **Yes.**
12:52:03 Q. **And self-administration?**
12:52:06 A. **Yes.**
12:52:06 Q. **And prefilled syringes that can be stored at room**
12:52:11 **temperature. Is that a convenience property?**
12:52:12 A. **Yes.**
12:52:13 Q. **And are there any other convenience properties than**
12:52:16 **those?**
12:52:18 A. **I think those there the main ones.**
12:52:20 Q. **Can you tell me which prior art bradykinin antagonist**
12:52:27 **peptides were self-administered?**

12:52:32 A. **Well, I mean, I think, as we discussed, it is the only**
12:52:35 **one that has been commercially launched. So the prior art**
12:52:40 **question is, are these attributes unique to icatibant over**
12:52:45 **what was known in the prior art. And I have relied on Dr.**
12:52:49 **Bachovchin regarding that.**
12:52:49 Q. **You don't know of any other bradykinin antagonist**
12:52:56 **peptide that was ever self-administered. Correct?**
12:53:01 A. **I am not aware of any other one that has been**
12:53:03 **commercially launched, no.**
12:53:04 Q. **You don't know of any that was ever administered to a**
12:53:06 **human, do you?**
12:53:08 A. **Better question for a technical expert.**
12:53:10 Q. **And you --**
12:53:12 **THE COURT: He is asking if you know.**
12:53:14 **THE WITNESS: I don't know.**
12:53:14 **BY MR. BLUMENFELD:**
12:53:15 Q. **Do you know any prior art bradykinin antagonist**
12:53:19 **peptide that can be stored at room temperature for years and**
12:53:24 **still be effective?**
12:53:27 A. **I am not aware of anybody undertaking the research to**
12:53:31 **do that one way or the other.**
12:53:32 Q. **When you look at the products that have been approved**
12:53:45 **by the FDA that are based on bradykinin antagonist peptides,**
12:53:52 **there is a class of one product. Correct?**
12:53:55 A. **In terms of what has been developed and commercially**

launched, I believe that's right.

Q. And that one product is Firazyr. Right?

A. That's correct.

Q. Now, you agree that Firazyr is effective in treating acute attacks of hereditary angioedema?

A. That's my understanding. I am not a clinician, but, yes.

Q. And you don't have an opinion as to whether icatibant is responsible for that effectiveness?

A. Not in any technical way, no.

Q. And you understand that Firazyr has been approved as a safe drug for the treatment of acute attacks of hereditary angioedema?

A. Yes, it's FDA approved as a safe and effective treatment.

Q. And you don't have any opinion as to whether that safety is due to the icatibant?

A. Not in any technical way, no.

Q. And the same with bioavailability, you understand that its a bioavailable product and that permits the subcutaneous administration?

A. I would defer to technical experts on that.

Q. You don't have an opinion as to whether that bioavailability is a property of the icatibant, do you?

A. Not in any technical way, no.

12:55:24 Q. **And the same with stability, you understand that it's**
12:55:27 **a stable product. Correct?**
12:55:29 A. **That's my understanding.**
12:55:29 Q. **And you don't have an opinion as to whether that**
12:55:32 **stability is provided by the icatibant?**
12:55:35 A. **I would defer to technical experts on that.**
12:55:37 Q. **You have looked at the labels of other products, of**
12:55:42 **Firazyr and other products, like Berinert and Kalbitor.**
12:55:45 **Right?**
12:55:46 A. **I have.**
12:55:46 Q. **Now, Kalbitor, its label, if you want to look at it,**
12:55:53 **is JTX-47, it has a black box warning that refers to**
12:56:00 **hypersensitivity reactions including anaphylaxis. You are**
12:56:06 **familiar with that. Right?**
12:56:07 A. **I am.**
12:56:07 Q. **And if you look at the Berinert label, again, that is**
12:56:14 **before you as JTX-21 if you want to look at it, it also**
12:56:18 **talks about hypersensitivity reactions, and having**
12:56:25 **epinephrine available. If you look up at the top right, the**
12:56:30 **very first line under Warnings an Precautions?**
12:56:35 A. **I see that.**
12:56:36 Q. **This is talking about Berinert, and it says Warnings**
12:56:39 **and Precautions, Hypersensitivity reactions may occur.**
12:56:44 **Epinephrine should be immediately available.**
12:56:45 **Do you see that?**

12:56:46 A. **I do.**

12:56:46 Q. **And you know epinephrine should also be available for**

12:56:51 **Kalbitor. Right?**

12:56:52 A. **Yes. I am not a clinician, but I understand that from**

12:56:55 **the label.**

12:56:55 Q. **That's because -- that's the reason that it's not**

12:57:00 **self-administered. Right?**

12:57:01 A. **Again, I am not weighing in as a clinician on that.**

12:57:04 **But that is my understanding from some of the documents.**

12:57:06 Q. **Now, you have looked at the Firazyr label. It doesn't**

12:57:10 **have a black box warning or a warning about hypersensitivity**

12:57:14 **reactions. Right?**

12:57:17 A. **I don't believe so, no.**

12:57:17 Q. **And you don't have any opinion whether it's icatibant**

12:57:23 **that's responsible for the absence of any warnings about**

12:57:28 **hypersensitivity reactions with Firazyr, do you?**

12:57:31 A. **I wouldn't be the one to weigh in on that. As I**

12:57:34 **explained, commercially, the documents explain that Shire**

12:57:37 **hasn't been able to differentiate on efficacy.**

12:57:40 Q. **Well, the absence of hypersensitivity reactions and**

12:57:53 **anaphylaxis is something that's important in Shire's ability**

12:58:01 **to sell Firazyr. Correct?**

12:58:05 A. **Well, I mean, as I explained earlier, what Shire**

12:58:09 **identifies as important to its sales is the convenience and**

12:58:13 **self-administration. The Shire marketing and commercial**

documents did not identify what you just described as, you know, the main differentiators. It was the convenience and self-administration.

Q. You pointed to JTX-13, and it's on Slide PDX-6.8. Do you remember that?

A. I do.

Q. And this is a Cowen & Company document. Right?

A. Yes.

Q. You quoted just a little bit of it on the slide about the "The FDA has indeed allowed for the inclusion of self-administration in the label. This is critical to the commercial success, as our consultants have previously referred to self-administration as the 'holy grail' for acute HAE treatment."

Do you see that?

A. I do.

Q. And the ability to self-administer Firazyr is because of the active ingredient icatibant. Isn't it?

A. Well, I mean, I think it's identifying the method of use. It's the formulation, combined with the active ingredient, and then looking at that all in the context of what was known in the prior art. But, yes.

Q. Can we put up JTX-13.1. I want to look at the rest of the sentence. Just put three lines up.

What it says in the part that you didn't blow up

was, "We believe that Firazyr now has the most differentiated formulation relative to other HAE treatment options on the U.S. market primarily due to the drug's stability at room temperature and subcutaneous self-administration."

Do you see that?

A. Yes.

Q. They said it was the most differentiated formulation relative to other HAE treatment options. Right?

A. I see that, yes.

Q. And they refer to stability at room temperature and subcutaneous self-administration. And all of those things are properties that result from the presence of icatibant in the Firazyr product correct?

A. Along with what I explained on direct, which I understand from Dr. Bachovchin are aspects which were previously known. But, yes.

MR. BLUMENFELD: Your Honor, I have no further questions.

THE COURT: Redirect.

MR. SHERRY: No redirect, Your Honor.

THE COURT: Thank you, sir. Be careful stepping down.

THE WITNESS: Thank you, Your Honor.

(Witness excused.)

13:00:55 **THE COURT: Do you rest?**

13:00:56 **MR. WIESEN: For the record, yes, Your Honor,**

13:00:59 **yes, Fresenius rests.**

13:01:00 **THE COURT: Let's talk about next steps,**

13:01:03 **counsel.**

13:01:07 **In terms of submission of proposed findings of**

13:01:10 **fact and conclusions of law, what is your proposal?**

13:01:13 **MR. BLUMENFELD: Your Honor, we did discuss this**

13:01:15 **last night. What we would propose, if acceptable to Your**

13:01:19 **Honor, is that we exchange 40-page submissions, one set, and**

13:01:26 **the date, because of trial commitments and other things, the**

13:01:30 **date that we were hoping would be acceptable to Your Honor**

13:01:33 **was March 20th.**

13:01:34 **THE COURT: I think that's probably going to be**

13:01:37 **too long.**

13:01:38 **MR. BLUMENFELD: Why --**

13:01:40 **THE COURT: How many days is that, Mr.**

13:01:42 **Blumenfeld? I was contemplating giving you 30 days.**

13:01:47 **MR. BLUMENFELD: That's a couple weeks longer**

13:01:49 **than 30 days. If you want it within 30 days, we will get it**

13:01:52 **to you in within 30 days.**

13:01:54 **THE COURT: That is what I need.**

13:01:55 **MR. BLUMENFELD: I think that comes to March 4.**

13:01:59 **THE COURT: Please have hyperlinks to the record**

13:02:01 **and to authority.**

13:02:03 I am not going to accept an appendix that
13:02:07 contains evidence that wasn't discussed in this trial.
13:02:11 Let's not do a document dump.
13:02:14 Anything else you need to cover?
13:02:16 MR. BLUMENFELD: The only thing, Your Honor, I
13:02:19 am trying to think in my mind what day of the week March 4th
13:02:22 is. If it is a weekend, which I think it may be, the next
13:02:27 business day after that?
13:02:31 I think it's a Sunday.
13:02:33 THE COURT: So the 5th.
13:02:35 MR. BLUMENFELD: That would be fine. Thank you,
13:02:36 Your Honor.
13:02:38 THE COURT: I am assuming that 30 days from
13:02:40 today works in terms of the availability of the transcript.
13:02:45 Mr. Maurer, is that do-able?
13:02:46 THE COURT REPORTER: Yes.
13:02:47 MR. BLUMENFELD: We discussed, also, and we will
13:02:50 discuss more, getting you a list of the admitted exhibits or
13:02:55 filing a list of the admitted exhibits, agreeing on that,
13:02:58 and also working on an errata to the transcript, which we
13:03:02 can get to Mr. Maurer.
13:03:03 THE COURT: Could you provide me with some
13:03:05 pictures of the witnesses as well.
13:03:06 MR. BLUMENFELD: Absolutely, Your Honor.
13:03:08 THE COURT: Of who testified, so that this

13:03:12 doesn't get too stale.

13:03:15 What's your collective, both of you, idea on the
13:03:20 relevance of secondary considerations in an obviousness-
13:03:27 type double patenting case?

13:03:28 MR. BLUMENFELD: Your Honor, this is an issue we
13:03:32 discussed at the pretrial. We are going to have a
13:03:35 difference of view on this. We know that.

13:03:38 THE COURT: That is okay. I am trying to get a
13:03:40 little bit of guidance as to your view.

13:03:42 MR. BLUMENFELD: In our view, in the Eli Lilly
13:03:45 case, Eli Lilly versus Teva, which was in the Federal
13:03:50 Circuit from an appeal, Your Honor, I think they clarified
13:03:52 that secondary considerations, including commercial success,
13:03:56 which was one of them there, apply in the obvious-type
13:04:02 double patenting situation. And that's true. It was in
13:04:05 that case and in many cases, even if the reference was not
13:04:12 publicly available.

13:04:13 In fact, if the reference was publicly
13:04:15 available, we would be talking about obviousness here, not
13:04:17 about obviousness-type double patenting. We think after Eli
13:04:23 Lilly and the case from Judge Stark, also, the UCB versus
13:04:26 Accord case, that secondary considerations apply here.

13:04:30 I think the Federal Circuit said in Eli Lilly
13:04:34 they must be considered.

13:04:34 THE COURT: It seems they said that. Mr.

13:04:39 Wiesen.

MR. WIESEN: Your Honor will remember, you may remember I was part of the team that tried that case.

13:04:45 THE COURT: I think I do remember that.

13:04:47 MR. WIESEN: We had argued at that time based on prior law that they were legally inapplicable.

13:04:53 THE COURT: You got me in trouble.

13:04:56 MR. WIESEN: I think we did. I apologize for that.

13:04:59 We are not arguing here that they are not legal -- they are legally inapplicable. The question is 13:05:01 whether they have established the nexus for this case. And 13:05:03 we think on that there is an absence of proof and therefore 13:05:07 in this case, for the two -- especially for commercial 13:05:10 success and long-felt need, there isn't a nexus.

13:05:15 I can imagine for example unexpected results, 13:05:19 you could compare the compounds to the '7,803 and icatibant, 13:05:22 and if there were unexpected results, use that secondary 13:05:26 consideration.

13:05:28 It is also the case that sometimes for 13:05:30 obviousness-type double patenting the reference is actually 13:05:32 prior art and there is also an obviousness-type double 13:05:36 patenting argument. You can imagine in a compound case, if 13:05:39 you can avoid the lead compound argument, as you do in 13:05:43 obvious-type double patenting but you don't in obviousness, 13:05:46

13:05:49 you might actually use a prior art patent for obviousness-
13:05:53 type double patenting. In that situation, it may be that
13:05:56 things like commercial success play in.
13:06:01 Here -- and we can argue it in the briefs --
13:06:03 certainly, we believe they have not established why the
13:06:06 economic or medical logic behind long-felt need and
13:06:10 commercial success would support those secondary
13:06:12 considerations being relevant.
13:06:14 THE COURT: I do know that.
13:06:18 Unless there is anything else, I wish you safe
13:06:21 travels home, counsel. Take care.
13:06:24 (Trial concluded.)

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